The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 130, No. 6 — CHICAGO, ILLINOIS — FEBRUARY 9, 1946

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TOXIC MANIFESTATIONS OF THIOURACIL THERAPY

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Increasing evidence of the usefulness of thiouracil in the treatment of thyrotoxicosis [1] has been accompanied by the appearance of many reports concerning the toxicity of this drug. Not infrequently these published reports refer to isolated cases or are unaccompanied by full numerical data from the series involved. It is possible, therefore, that they may give an erroneous impression of the frequency of toxic reactions. Before the usefulness and final place of this drug can be settled, we must be able to balance its toxic manifestations against its pharmacologic advantages, and for this reason an accurate estimate of the incidence of severe toxic manifestations in patients under treatment with the drug should be a useful adjunct to our knowledge.

Therefore it has seemed advisable to gather together data from a large group of patients treated with thiouracil so that the actual incidence of toxic manifestations might be studied in relation to the total number of patients treated. In this way accurate statistics on the expected incidence of toxic reactions should be obtained. To accomplish this end the present group of eleven clinics in this country and one in England have accumulated their joint experience with toxic reactions, and these data are herewith presented. It should be stressed that this material is presented in an attempt to arrive at an accurate figure for the incidence of toxic reactions; it is not in any sense an appraisal of the usefulness of thiouracil or an attempt to define the limits of its applicability. Nor is it, further, an attempt to settle the present controversy as to whether this drug should be used as a treatment of thyrotoxicosis per se or in the preoperative preparation of patients for thyroidectomy.

It is of interest that the preparation of patients for surgery can usually be accomplished with this drug in eight weeks or less, and therefore the additional question presents itself of the time relationships of various toxic reactions. An attempt at analysis with respect to these factors will also be presented.

A further consideration in the method of analysis used has been the fact that thiouracil appears to have one potentially fatal toxic manifestation, that concerned with an effect on leukocyte production. Unlike the sulfonamides, thiouracil appears to carry only this major hazard at the present time. It is true that severe hepatic damage has been reported and several instances occurred in the present series of patients, but thus far these lesions have not proved fatal and have been amenable to the usual forms of treatment. The present effort has been to obtain accurate data on the incidence of the hematologic reactions rather than a tabulation of the host of other less dangerous reactions which may occur also with thiouracil and which doubtless will continue to be reported in new forms as time goes on. For this reason the incidence of agranulocytosis and leukopenia are the chief concerns of this investigation. The statistics concerning drug fever, skin eruptions, psychotic manifestations, lymph node enlargement, salivary gland disorders, hepatic damage and other reactions have not been stressed, and the data on these reactions are not intended to be definitive.

These cases include many of the first in which treatment with thiouracil was administered, and, as experience grows, means of avoiding these reactions may become evident.

1. A partial bibliography of recent articles dealing with thiouracil and thiouracil toxicity: Astwood, E. B.: Treatment of Hyperthyroidism with Thiourea and Thiouracil, J. A. M. A. **122**: 78-81 (May 8) 1943. Barr, D. P., and Shorr, E.: Observations on the Treatment of Graves' Disease with Thiouracil, Ann. Int. Med., to be published. Bartels, E. C.: Thiouracil: Its Use in the Preoperative Management of Severe Hyperthyroidism; Preliminary Report, J. A. M. A. **125**: 24-26 (May 6) 1944. Clute, H. M., and Williams, R. H.: Thiouracil in Preparation of Thyrotoxic Patients for Surgery, Tr. Am. S. A. **62**: 504-513, 1944. Ferrer, M. I.; Spain, D. M., and Cathcart, R. T.: Fatal Agranulocytosis Resulting from Thiouracil, J. A. M. A. **127**: 646-647 (March 17) 1945. Himsworth, H. P.: Thyrotoxicosis Treated with Thiourea, Lancet **2**: 465-466, 1943. Himsworth, H. P., and Joll, C. A., in discussion on Thiouracil and Thiourea in Treatment of Thyrotoxicosis, Proc. Roy. Soc. Med. **37**: 693-704, 1944. Kahn, J., and Stock, R. P.: Fatal Agranulocytosis Resulting from Thiouracil, J. A. M. A. **126**: 358-359 (Oct. 7) 1944. Linsell, D.: Agranulocytosis After Use of Thiouracil, Brit. M. J. **2**: 597-598, 1944. McArthur, J. W.; Rawson, R. W., and Means, J. H.: Idiosyncratic Febrile Reaction to Thiouracil, Ann. Int. Med., to be published. McGavack, T. H.; Gerl, A. J.; Vogel, M., and Schwimmer, D.: The Treatment of 26 Thyrotoxic Patients with Thiouracil and a Review of Toxic Reactions in All (135) Reported Cases, J. Clin. Endocrinol. **4**: 249-261, 1944. Meyer, A. H.: Granulocytopenia: Case Caused by Thiouracil, California and West. Med. **61**: 54, 1944. Moore, F. D.; Sweeny, D. N., Jr.; Cope, O.; Rawson, R. W., and Means, J. H.: The Use of Thiouracil in the Preparation of Patients with Hyperthyroidism for Thyroidectomy, Ann. Surg. **120**: 152-169, 1944. Newman, E. V.: Thiouracil and Hyperthyroidism, M. Clin. North America **29**: 302-322, 1945. Paschkis, K. E.: Thiouracil in Treatment of Thyrotoxicosis, ibid. **28**: 1362-1375, 1944. Paschkis, K. E.; Cantarow, A.; Rakoff, A. E.; Walking, A. A., and Tourish, W. J.: Thiourea and Thiouracil in Treatment of Thyrotoxicosis, J. Clin. Endocrinol. **4**: 179-184, 1944. Riker, W. F., and Wescoe, W. C.: The Pharmacology and Therapeutic Applications of Anti-Thyroid Compounds, Am. J. M. Sc., to be published. Rubinstein, M. A.: Thiouracil Therapy: Agranulocytosis Following Administration, Am. J. Clin. Path. **14**: 540-543, 1944. Werner, S. C., and Elliott, R. H. E., Jr.: Thiouracil in the Treatment of Postoperative Recurrent Toxic Goiter, Bull. New York Acad. Med. **20**: 417, 1944. Williams, R. H., and Clute, H. M.: Thiouracil for Thyrotoxicosis, J. A. M. A. **128**: 65-69 (May 12) 1945.

In table 1 is shown a list of the clinical groups cooperating in this study and the number of patients treated by each group.[2]

The accumulated experience of this group of clinics comes to a total of 1,091 patients, a number which is probably large enough so that the incidence of toxic manifestations during thiouracil therapy may be regarded as statistically significant. The length of time during which these patients were under treatment covers a broad range from patients treated two weeks (less than 1 per cent of the series) to a very few patients treated for periods up to two years or more. The great majority of the patients were treated between two and eight months. The dosages have been variable, but they have varied within a fairly narrow range and, as will be seen later, do not materially affect the analytic results. Most of the clinics have employed 0.5 to 0.8 Gm. a day for a period of three to seven weeks or until the basal metabolic rate fell to normal or nearly normal levels. The dosages have then been cut to 0.2 to 0.4 Gm. per day, and those clinics which have carried the patients on for many months without surgery have further cut the dosage to as low as 0.1 Gm. or less per day or every other day. The clinics which have employed

TABLE 1.—*Number of Cases Treated at Cooperating Clinics*

Barnes Hospital and Washington University School of Medicine, St. Louis	62
Beth Israel Hospital, Boston	63
Boston City Hospital and Massachusetts Memorial Hospitals, Boston	225
Jefferson Medical College, Philadelphia	55
Johns Hopkins Hospital, Baltimore	45
Lahey Clinic, Boston	196
Massachusetts General Hospital, Boston	99
Mayo Clinic, Rochester, Minn.	38
New York Hospital, New York	125
Presbyterian Hospital, New York	88
University College Hospital Medical School, London, England	64
University of California Medical School, San Francisco	31
	1,091

the drug largely as a preparation for surgery have tended to maintain higher dose levels, but for a shorter period of time; one group reports an average duration of preoperative treatment of fifty-seven days in the first 100 cases. The practice of the clinics with respect to surgery differs considerably and is not important for the purposes of this report. Three of the groups have used the drug solely as a preoperative treatment, three have used it predominantly as a treatment for thyrotoxicosis without surgery and the rest have either varied their practice from time to time or have consistently divided their cases into two groups.

FATALITIES

In table 2 is shown the incidence of fatal outcome during the administration of thiouracil. In the 1,091 treated cases there were eight deaths which occurred during the administration of the drug. A brief account of these deaths follows:

CASE 1.—A person suffering from severe toxic diffuse goiter (metabolic rates starting in the range of +56) and severe myasthenia gravis developed fever and a severe exacerbation of the myasthenic state on the eleventh day of treatment. The patient died on the following day, a typical myasthenic death. Although the drug may have been responsible for the fever, it is probable that the death should be regarded as a myasthenic death and not a death due to the drug itself, as the fever would probably not have been fatal in a thyrotoxic patient without myasthenia.

CASE 2.—A person with severe myasthenia gravis, who had relatively mild toxic diffuse goiter, was given the drug for two months, at which time death took place, the death being that of fatal myasthenia gravis. There was no leukocyte-depressing action of the drug. This again should not be considered a drug death.

TABLE 2.—*Deaths Under Thiouracil Administration*

Total Cases Treated	Total Deaths		Drug Deaths	
	Number	Per Cent	Number	Per Cent
1,091	8	0.73	5	0.46

CASE 3.—A middle-aged person who had developed a mild neutropenia on thiouracil was continued on the drug with the occurrence of agranulocytosis. This was treated by stopping the drug and administering vigorous systemic therapy. Four days after the polymorphonuclear count began to rise, the patient developed a cerebral thrombosis and died ten days following the cessation of thiouracil therapy. Although the cause of death is mixed in this case, it may be counted as a drug death, as it followed the development of agranulocytosis and was a complication of that condition (table 5, case 13).

CASE 4.—A person with severe arteriosclerotic heart disease, angina pectoris, pernicious anemia and thyrotoxicosis died a cardiac death and at postmortem examination extensive myocardial damage was found, consistent with a long history of coronary disease. Microscopic examination disclosed perivascular infiltrative lesions not unlike those found by Rich [3] following serum sickness and sulfadiazine poisoning and also reported by Marine and Baumann [4] in thiouracil fed rats. The role of thiouracil in this fatal outcome was doubtless of secondary importance in a complex situation, but the histologic changes suggest that tissue sensitivity phenomena may occur during the administration of thiouracil. This case is not considered to be a drug death.

CASE 5.—A woman under treatment with thiouracil for thirty-five days was given a dosage of 0.6 Gm. per day. After an initial period of regulation of her thyrotoxicosis in the hospital she was discharged home to be followed by her physician. After thirty-five days of therapy the patient complained of a sore throat. She died five days later of typical agranulocytosis with agranulocytic angina, despite vigorous treatment instituted after the recognition of the syndrome. This is considered to be a drug death [5] (table 5, case 9).

CASE 6.—This was the third course of thiouracil administered to this thyrotoxic patient during a period of one year. Thirty days following the initiation of thiouracil treatment and while on a dosage of 0.2 Gm. of thiouracil a day, the patient developed a sore throat, followed by a severe shaking chill and a temperature of 103.5 F. Thiouracil was omitted and the patient was hospitalized the following day. On the sixth hospital day the patient died of agranulocytosis. This death is regarded as due to the drug [6] (table 5, case 5).

TABLE 3.—*Incidence of Agranulocytosis*

Total Cases Treated	Agranulocytosis	
	Number	Per Cent
1,091	19	1.74

2. The collector of these data wishes to express his appreciation to the physicians in these many clinics for their readiness to pool their experiences and data on thiouracil toxicity so that an analysis of the whole series might be accomplished. This provides a more comprehensive survey than could be accomplished by any one clinic alone.

3. Rich, A. R.: Additional Evidence of Role of Hypersensitivity in Etiology of Periarteritis Nodosa and Case Associated with Sulfonamide Reaction, Bull. Johns Hopkins Hosp. **71**: 375-379, 1942.

4. Marine, D., and Baumann, E. J.: Periarteritis Nodosa-like Lesions in Rats Fed Thiouracil, Arch. Path. **39**: 325-330, 1945.

5. Bartels, E. C., and Blizard, E. C.: Toxic Reactions to Thiouracil, Lahey Clin. Bull. **4**: 150-158, 1945.

6. Gargill, S. L., and Lesses, M. F.: Toxic Reactions to Thiouracil, J. A. M. A. **127**: 890-898 (April 7) 1945. Lesses, M. F., and Gargill, S. L.: The Effect of Thiouracil on the Blood, with Especial Reference to Neutropenia and Agranulocytosis, New England J. Med., to be published.

CASE 7.—A woman received 65.2 Gm. of thiouracil in fifty-three days, a dosage unusually large because she had previously received iodine treatment and was resistant to thiouracil therapy. Agranulocytosis was diagnosed fifty-seven days after thiouracil was begun and the drug was then stopped. Starting about fourteen days before the thiouracil was stopped, the patient had a furuncle on the nose and about a week later she started to develop a paronychia. Terminally there was bronchopneumonia and a lung abscess. This must be considered a drug death; granulocytopenia was accompanied by widespread infectious manifestations (table 5, case 18).

CASE 8.—A woman received 13.8 Gm. of thiouracil in thirty-six days. She was being treated outside the hospital and reported to her private physician with pneumonia and granulocytopenia, which were fatal. This also is considered to be a death due to the drug (table 5, case 10).

These data leave us with a figure for death under thiouracil administration of 0.7 per cent and death directly attributable to the drug of 0.5 per cent.

AGRANULOCYTOSIS

In table 3 is shown the incidence of agranulocytosis during thiouracil therapy. In this table the term "agranulocytosis" is used in the strict sense to mean depressed or absent neutrophilic cells with the concomitant picture of infection, usually around the neck, throat and floor of the mouth. The term is not employed unless the patient showed evidence of agranulocytic "angina" or sepsis elsewhere concomitant with a decided granulocytopenia. There were 19 such cases, the details of which are shown in table 5.

TABLE 4.—*Incidence of Leukopenia*

Total Series Reporting	Leukopenia	
	Number	Per Cent
781	27	3.4

With the exception of 3 patients who had previous thiouracil therapy, accounting for a possible degree of sensitization, the great majority of these cases of agranulocytosis occurred between four and eight weeks of therapy. There was one delayed case at thirty-six weeks. Of the 19 cases, therefore, 15, or 79 per cent, occurred during the second month of treatment, and 18 out of 19, or 95 per cent, occurred in eight weeks or less after the initiation of treatment. No exact quantitative relationships can be discerned between the total amount of drug employed and the onset of agranulocytosis, as some patients developed severe granulocyte depression on as little as 4.2 Gm. of the drug and others required as much as 65.2 Gm. However, it is important to stress that it is not the total amount of thouracil administered but rather the period over which it has been administered which determines the "period of maximal danger" or "period of maximal neutropenic incidence." This phase, when the patient is most apt to develop a potentially fatal complication, is between four and eight weeks of treatment, and during this stage of therapy the patient should be followed with extreme care. However, it should be emphasized, since the overall spread in the incidence of agranulocytosis runs from two weeks to thirty-six weeks, that throughout treatment the patient must be followed with reasonable clinical precautions.

Previous thiouracil administration tends to hasten the onset of this "period of maximal neutropenic incidence." Four out of 19 cases of agranulocytosis had had previous thiouracil therapy. Therefore, it is conceivable that sensitization by previous administration may at times be an important etiologic factor in the development of agranulocytosis.

As the 5 deaths which were reported as directly attributable to the drug occurred as a result of agranulocytosis, the mortality rate for agranulocytosis is 5 out of 19, or approximately 26 per cent, in this series.[7]

Two patients developed agranulocytosis while on thiouracil and a sulfonamide simultaneously. The avoidance of this combination would appear to be justified as a general policy, since either drug alone may depress leukocyte production.

TABLE 5.—*Patients Developing Agranulocytosis*

Case	Duration of Treatment	Comment
1	2 weeks	Previous thiouracil therapy; possible agranulocytosis during previous treatment at other institutions
2	2 weeks	Previous thiouracil therapy six months ago; present dose 0.2 Gm. per day; WBC 4,900, PMN 8%; sore mouth; borderline case [8]
3	3 weeks	Previous thiouracil therapy six months ago; present dose 0.2 Gm. per day; WBC 600, granulocytes 0%; severe pharyngeal manifestations; recovered with intensive penicillin therapy after 7 days of complete agranulocytosis [8]
4	4 weeks	Dose 0.6 Gm. per day; WBC 3,100, PMN 0%; typical pharyngeal manifestations
5	4 weeks	Previous thiouracil therapy on two occasions within a year; dose 0.2 Gm. per day, 3 months, first course; 0.2 Gm. per day, 3½ months, second course; present dosage 0.2 Gm. per day; had been discharged from hospital; WBC 1,000, PMN 0%; severe pharyngeal manifestations; bone marrow biopsy showed hypoplastic marrow; died on 6th day of agranulocytosis [6]
6	4 weeks	Patient developed fever and pharyngeal inflammation 8 days after stopping thiouracil; WBC 900, PMN 0% [5]
7	4 weeks	Mild systemic reaction with early agranulocytic angina; WBC 1,600, PMN 7% [5]
8	4 weeks	Angina pectoris treated with thiouracil 0.8 Gm. per day 7 days, 0.6 Gm. per day 18 days, 0.4 Gm. per day 2 days; WBC 2,100, PMN 7%; borderline case [6]
9	5 weeks	Dose 0.6 Gm. per day; had been discharged from hospital; sore throat first symptom; WBC 1,000, PMN 0%; Died on 5th day of disease [5]
10	5 weeks	Dose 0.3 Gm. per day for 25 days, 0.2 Gm. per day for 11 days; pneumonia with concomitant agranulocytosis and agranulocytic angina; fatal outcome
11	6 weeks	Concomitant sulfadiazine therapy for pneumonia; dose 0.9 Gm. per day 40 days, 0.6 Gm. per day 6 days; PMN 0%
12	6 weeks	Dose 0.8 Gm. per day; a 70 year old patient who showed a poor response to thiouracil; also had diabetes mellitus
13	6 weeks	Agranulocytosis apparently successfully treated by stopping the drug and administering intensive therapy; cerebral thrombosis at the time that blood count began to rise; death 10 days following cessation of thiouracil treatment
14	6 weeks	Mild agranulocytosis; recovery [5]
15	6 weeks	0.6 Gm. per day for 14 days, 0.4 Gm. per day for 14 days, 0.2 Gm. per day for 14 days; fever, infected fingers; PMN greatly reduced for 7 days (Williams, R. H., and Clute, H. M.: New England J. Med. **230**: 657, 1944)
16	7 weeks	
17	8 weeks	Concomitant sulfathiazole therapy
18	8 weeks	Dose 1.5 Gm. per day for 37 days, 0.6 Gm. per day for 16 days; unusually large dose of thiouracil in patient apparently resistant to treatment; granulocytopenia with angina, furuncle on nose, paronychia, bronchopneumonia, lung abscess; fatal
19	36 weeks	

LEUKOPENIA

In table 4 is shown the incidence of leukopenia during the administration of thiouracil. In this table the term "leukopenia" is used to denote depression of the white cell series without the development of infection around

7. One additional instance has been reported which is of interest in this connection. The patient received thiouracil for about three weeks and then developed a leukopenia. The drug was stopped and two weeks later she developed granulocytopenia and a temperature of 106 F., with cellulitis and lymphangitis of the finger, extending up to the axilla. During this time, her white blood count fell to 400. She was treated with penicillin and transfusions and ultimately recovered. It is difficult to reconstruct all the events leading up to this situation, but in view of the leukocyte depression produced two weeks previously by thiouracil, one may place the blame for the failure of leukocyte response at least in part on thiouracil. If this is true, it would suggest that any patient who has developed a neutropenia on thiouracil should be followed closely for approximately another month and advised as to the dangers of intercurrent infection.

the throat or floor of the mouth or elsewhere and in which the selective depression of the neutrophilic series is not as striking as in the cases of agranulocytosis. This table includes cases only from those series in which the incidence of leukopenia was indicated numerically. Most of the clinics regarded any reduction of white cell count to less than 3,000 as significant. The polymorphonuclear cells were usually somewhat reduced, though rarely below 10 per cent, and in some cases they remained as high as 50 per cent.

It is significant that no leukopenias were reported as occurring less than twenty-five days after the initiation of treatment, with the one exception of a patient previously treated with thiouracil without reaction. The majority of the leukopenias occurred at four to six weeks of treatment. In many of these cases the white cell count returned to normal without ceasing administration of the drug. In the majority of them, however, the drug was stopped and again a return to normal without other specific therapy was the rule. It is worth stressing that here again, just as in the agranulocytoses, the "period of maximal leukopenic incidence" is from four to eight weeks after the initiation of treatment.

DRUG FEVER

In table 6 is shown the incidence of drug fevers in this group of cases, and only those series in which the incidence of fever was definitely recorded are included

TABLE 6.—*Incidence of Drug Fever*

	Drug Fever	
Total Series Reporting	Number	Per Cent
781	38	4.9

in this tabulation. In all of these cases except 4 the drug was known to be definitely the cause of the fever, usually as demonstrated by the administration of subsequent "pilot" doses. It is of interest that one of these drug fevers, subsequently proved to be due to the drug, occurred only five hours after the initial administration of the drug. This suggests preexistent sensitization from some unknown source, a factor which might, in isolated cases, hasten the onset of leukocyte-depressing reactions also. All of these drug fevers are early manifestations and with only two exceptions they occurred under four weeks of therapy. The dosages employed did not vary significantly between those clinics reporting fevers and those few groups which included a very low incidence or absence of fever. The latter were all small groups of patients in which the laws of probability might be responsible for the reported absence of drug fever.

MISCELLANEOUS REACTIONS

Other toxic reactions of a wide variety were reported from a number of clinics. As previously mentioned, a detailed analysis of these miscellaneous and variable reactions has not been an important part of this joint effort. However, a brief statement of the data which are available is as follows:

Ten cases of lymph node or glandular enlargement were reported in a total of 458 cases in series reporting the presence or absence of this complication. These glandular enlargements included disorders in the various salivary glands as well as the lymph nodes in the neck. One case of thyroiditis was reported. Two cases of acute parotitis were reported in this series. Many of these reactions disappeared with continuance of the drug and none of them was of special severity. One case of "Mikulicz syndrome" was reported with swelling of the parotid glands, the submaxillary glands and the tear glands. Possibly a related phenomenon was the occurrence of conjunctivitis in another patient.

One clinic reported several cases of oral sepsis associated with administration of the drug but unassociated with white cell depression. These were cases of dental abscesses, gingivitis, sore throat and stomatitis without agranulocytosis, which seemed to undergo exacerbations while under treatment with the drug. An exact causal relationship could not always be established. The drug was not stopped in most of the cases.

Various groups reported skin reactions, edema of the feet, jaundice and psychotic manifestations as isolated happenings. Albuminuria in several cases and 1 case of hematuria represent the only renal complications reported. The albuminurias appeared to be of little significance. The hematuria occurred without crystalluria and could have been due to causes other than the drug.

One case of platelet depression to 32,000 with positive Rumpel-Leeds test occurred after twelve days of treatment. The bleeding time was normal, the clotting time increased to 20.5 minutes (Lee and White test). Check platelet counts and smear confirmed this situation. Within forty-eight hours of withdrawal of the drug the platelet count rose to normal levels. Subsequent administration of thiouracil (ten days later) to the same patient failed to alter the platelet count.[8]

The occurrence of mild and occasionally profound myxedema has been observed in patients in whom treatment has been allowed to depress the metabolism to a low level. During this phase, if the patient is prepared for operation with the usual preoperative medication, unusual sensitivity to opiates may be observed which must be regarded as one of the hazards of thiouracil administration.

Two "scleroderma-like" reactions have been observed in which the patient developed tightness of the skin and a sensation of muscle binding. Objectively they showed loss of skin mobility and elasticity, but little else. Both these patients had been treated for sixty-five to seventy-five days and both of them were mildly hypothyroid.[5]

SUMMARY

A joint study of the incidence of severe toxic reactions during thiouracil therapy has been completed by eleven clinics in various parts of the United States and one in England. One thousand and ninety-one patients were treated in these institutions up to the time of reporting their data (which was generally completed about April 15, 1945).

The series reported includes patients treated for periods of from two weeks to two and one-half years. The dosages employed were generally from 0.5 to 0.8 Gm. per day for a period of three to seven weeks or until the basal metabolic rate was normal, following which the dose was either reduced or the patient was operated on. Minor variations in this dosage routine were employed by many of the clinics and do not significantly alter the statistics. The following summary of the data here presented is offered, using round numbers to express incidence:

1. Death under administration of the drug, 0.7 per cent.
2. Death attributable directly to the drug, 0.5 per cent.
3. Agranulocytosis, 1.8 per cent.

8. Barr, D. P.: Thiouracil in the Treatment of Thyrotoxicosis, New York Med. **1**: 17, 1945.

4. Death rate in agranulocytosis, 26 per cent.
5. Leukopenia without agranulocytic angina, 3 per cent.
6. Fever, 5 per cent.
7. Glandular enlargement, 5 per cent.
8. Miscellaneous reactions, 2 per cent.

Of these reactions agranulocytic angina, leukopenia and high fever all make cessation of drug administration virtually mandatory. The total incidence of these reactions is between 8 and 10 per cent. These data would indicate that approximately 1 out of 10 patients in whom treatment was started had to have the treatment stopped because of the incidence of a reaction which could not be handled safely without discontinuance of the drug. This is a maximal figure, as some of the leukopenias may be treated with continuance of the drug, although there is some evidence to indicate the possible danger of such a course. On the basis of these figures, approximately 2 out of every 100 patients treated may be expected to develop agranulocytosis. If this reaction is identified and diagnosed immediately and drastic treatment begun, the death rate may be lowered below the figure of 26 per cent observed in this early series of cases. The data here presented lead to the conclusion also that previous thiouracil therapy or concomitant sulfonamide therapy appears to increase the risk of leukocyte depression and therefore enforce careful observation and the utmost caution in the handling of patients.

The treatment of agranulocytosis falls beyond the scope of this report; all those who have had experience with this complication stress that early and adequate penicillin therapy is of the utmost importance in controlling the infectious manifestations.

The most dangerous period from the point of view of leukocyte depression is from four to eight weeks after initiation of treatment. The onset of this period may be lowered to two weeks, if the drug has been administered previously to the same patient, regardless of whether or not there was untoward reaction on the previous occasion. During this "danger period," any patient under treatment with thiouracil should be followed with extreme care and caution, and the isolated incidence of toxic reactions up to nine months of therapy make continued supervision essential.

COMMENT

DR. DAVID P. BARR, New York: It is not apparent that the size of the dose or the method of administration will insure against toxic reactions. It is evident that agranulocytosis will appear with disarming suddenness. It is unlikely that even frequent blood counts will give a sufficient warning. At least equally important is the education of the patient to symptoms which may indicate the beginning of agranulocytosis and a liability to infection. As our study has gone on, we have had to depend more and more on the cooperation of the patient in detecting evidence of toxicity. All will agree that early diagnosis of agranulocytosis is crucial. Our own experience with one case of great severity has suggested to us that a patient may be protected for many days during complete agranulocytosis from overwhelming infection by adequate use of penicillin.

DR. H. P. HIMSWORTH, London: If leukopenia is arbitrarily defined as a level of white blood corpuscles lower than 3,000 per cubic millimeter, then it is quite correct to say that thiouracil does not produce leukopenia in more than a minority of patients. But if the white blood cell count after treatment is compared with the white blood cell count before treatment in the individual patient, it has been our experience that a fall occurs in most cases. In further support of this view is our observation that the Arneth count swings to the left under thiouracil therapy. This depression is related to dosage. With 0.8 Gm per day the white blood count falls. When the dose is lightened to 0.2 or 0.1 Gm. the level rises to approximately the value before treatment. Thereafter a slow decline spread over many months occurs in many patients, although it is only in very few that the level falls ultimately below 3,000. These observations were undertaken in the hope that we might be able to detect potential cases of agranulocytosis before symptoms developed. In this respect they have failed. There has been nothing unusual about the fall in the white cells in those of our cases in which agranulocytosis has developed or in most of those in which leukopenia has developed. In both instances the condition has appeared suddenly and in the former appears to have been related to an intercurrent infection. The practical points which arise from these results are that a fall in white blood cells occurs in most patients under thiouracil therapy and is not necessarily an alarming feature. Routine white blood cell counts should be done on all patients to detect unsuspected leukopenia; but it cannot be assumed that, if the white cell level is normal, the patient will not develop agranulocytosis even in the immediate future. All patients, irrespective of the levels of their white cells, should be instructed to omit thiouracil and report at once if any febrile illness develops.

DR. KARL E. PASCHKIS, Philadelphia: Since this report was submitted we have made further observations which appear of interest. We have observed 2 cases of agranulocytosis other than those described in this report. In both cases there was associated liver damage, as evidenced by jaundice and abnormal sulfobromophthalein retention. Whether the liver damage was a result of the concomitant infection or whether the liver damage played a part in the pathogenesis of the agranulocytosis cannot be decided. Evidence of liver damage was also observed in 2 other patients who had drug fever due to thiouracil but no agranulocytosis. Evidence of liver damage would probably be found more frequently in cases of toxic reaction to the drug, both with and without agranulocytosis, if serum bilirubin determinations and liver function studies were carried out routinely in such cases.

In 2 cases of agranulocytosis recovery followed (1) withdrawal of the drug, (2) treatment with penicillin and (3) administration of crude liver extract and of pyridoxine. We believe that withdrawal of the drug and combating the concomitant infection are essential. How much the adjunct treatment with liver and vitamin B_6 actually contributed to the cure cannot be decided. After recovery both these patients received test doses of thiouracil. One tolerated the drug, whereas the other developed leukopenia and neutropenia.

Another case of interest is that of a man with thyrotoxicosis recurring ten years after subtotal thyroidectomy. On admisssion he had a leukopenia of 2,500 to 3,000, with 35 to 39 per cent of polymorphonuclears. Review of his previous hospital record showed that the leukopenia had been present at the time of the original thyroidectomy (ten years before). Thiouracil has been tolerated by this patient, his blood count and bone marrow showing no appreciable change on repeated examination over a period of five months.

Effects of Closed Cranial Injuries.—The clinical effects of injury to the upper brain stem are not always to be clearly distinguished. In the cases with short survival periods, the specific symptoms and signs pointing to a disturbance of functions of this region are obscured by traumatic shock, by deep coma and by the effects of other associated lesions of the brain. Particularly in the case of unilateral distorting lesions with longer survival periods, the progressive development of unilateral motor signs and deepening stupor also befog the situation until late in the progress of the intracranial situation when the vital centers begin to fail. Nevertheless, the alert and persistent examiner can often find evidences of such disturbances. These symptoms may be divided into three groups: those referable to the vital functions (maintenance of respiratory and circulatory functions), pupillary changes and motor symptoms. Since the pupillary changes are but incidental, the essential syndromes will concern the vital and motor functions.—Courvill, Cyril B.: Effects of Closed Cranial Injuries on the Midbrain and Upper Pons, in Trauma of the Central Nervous System, Baltimore, Williams & Wilkins Company, 1945.

CHRONIC BRUCELLOSIS: SUCCESS OF TREATMENT WITH BRUCELLIN

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Pasteurization of every drop of milk produced today would effectively reduce to the minimum tomorrow's new cases of brucellosis in all but the few occupations concerned with handling of infected animals. However, if such a forward step could be taken to protect the general population now, it would scarcely affect thousands of persons who drank raw milk several years ago. Eradication of infection in dairy herds to prevent new cases presents many difficulties. The diagnosis and treatment of thousands of old chronic cases presents many more problems. Of course pasteurization is not yet universal. Travel between the states has increased since 1941. Early in the mobilization after Pearl Harbor certain training units in the field were obliged to purchase food for mess, including raw milk, wherever it could be found. Officers and men could thus easily have contracted brucellosis while in service. Then and now they are still unprotected from possible exposure while on furlough.

Actually the dairy industry is hard at work to eliminate brucellosis in milk producing animals, even while all such milk products are requisitioned by a wartime economy. Nearly 40,000 calves were vaccinated in the United States in the one month of April 1944. During the same month over 13,000 cattle slaughtered had been found previously to be positive reactors by blood test.[1]

Meanwhile members of the profession everywhere, both civilian and military, must remain alert to an infection especially of the milder chronic type whose beginning is so often masked or insidious. Repeated attention has been called to the appearance in this country of the more dramatic acute febrile forms of infection. It was the presentation sixteen years ago by Simpson and Frazier [2] which was directed to the largest medical audience and summarized the problem well. Yearly increases of reported cases followed. The diagnosis in such a protean disease must at any time be considered by the internist, gastroenterologist, orthopedist, neuropsychiatrist or general practitioner.

Extended use of the means of detection are being made. An appraisal of the diagnostic methods (1) clinical history, (2) blood culture, (3) serum agglutination, (4) opsonic index and especially (5) the intradermal skin test, together with (6) the therapeutic test, is my purpose in this paper.

The prevalence by survey of latent, subclinical forms of brucellosis is astonishingly high. Reasonable doubt that the health problem so represented is indeed serious might be entertained if the efficacy of tests used in such a survey could be questioned or if such figures indicated merely active immunity. But in truth a most widely disseminated, highly invasive and extremely tenacious organism is concerned. Therefore a mammoth reservoir of potential danger to national health and efficiency is at hand.

Angle [3] found the incidence by skin test in 7,122 school children to be 9 per cent. The high was actually 18 per cent in the group of 711 oldest children and among those who came largely from families which kept cows of their own. It was lowest, 1 to 2 per cent, in the Negro families which bought milk in bottles at stores. Although city dwellers are indeed often exposed, rural populations are in greatest danger. There are 57,245,000 persons living in small towns and in rural areas of the United States. Nine or even 1 per cent of such a population total, or that of any one of the several states, produces an impressive figure. Among these must certainly be some who are immune, but the rest may be ill at this time or, since the disease can last a lifetime, destined to develop symptoms at some future date. It will appear from this study that such high percentages are not absurd but reflect the tenacity of Brucella (chiefly the abortus variety), and that suffering and time lost by illness is great, but that treatment is effective if the cause is recognized.

Bacteremia may be demonstrated early in the course of many cases with fever, but the diagnosis rests chiefly on serologic and skin tests, especially in the chronic state. Blood culture requires special mediums held beneath atmospheres of 15 to 20 per cent carbon dioxide. Rarely is blood culture found positive in the chronically ill, but the significance in any case is obvious. The opsonophagocytic index is a somewhat difficult and rather needless laboratory aid for routine use.

Agglutinins begin to appear several days to several weeks after onset. For the physician the agglutination test is simply a matter of drawing blood as for a Widal or Kahn test, this to be sent to a competent laboratory. The titer in the serum may reach a height of 1 : 5,000 but is roughly proportional to the highest recorded elevation of temperature between 99 and 105 F. Attention must be paid to low titers, and anything above 1 : 40 is diagnostic. Specificity of the test is high, with false positives almost nil, the only important cross agglutination being in tularemia. Sensitivity is not very high, however, at least in relation to the antigen in use at present. Agglutination has been found negative at times when the blood culture was positive. Agglutinins if present at the onset often disappear as the infection persists, so that negatives result in at least 46 per cent of the chronically affected according to Evans,[4] and in 86 per cent according to Huddleson.[5] Such results almost invalidate the test as a diagnostic measure in the ambulatory case.

The peculiarities of the proteins of the brucella cell structure must account for the inconsistencies of the agglutinin response on single tests. Heat stable endotoxin comprises roughly 25 per cent of the cell and is accompanied by a relatively large amount of toxin enhancing lipoid. The endotoxin in man as in experimental animals produces the systemic effects of hyperglycemia followed by hypoglycemia; elevated, then lowered basal metabolism; leukopenia; subnormal temperature, and so on. This endotoxin appears to stimulate as an antigen little if any antibody. The low antigenicity may largely account for the ability of the organism to live on unharmed by the host. Brucellosis cannot be said to be self limiting.

The function of the intradermal test is to detect the presence of endotoxin in the circulation. Skin sensitivity, after bacteremia and agglutinin response, if any, is the last to appear and the last to disappear. By the

From the Sansum Clinic.

1. Summary of Brucellosis (Bang's Disease) Work in Cooperation with the Various States, United States Department of Agriculture, April 1944.
2. Simpson, W. M., and Frazier, E.: Undulant Fever: Report of 63 Cases Occurring In and About Dayton, Ohio, J. A. M. A. **93**: 1958-1963 (Dec. 21) 1929.
3. Angle, F. E.; Algie, W. H.; Baumgartner, L., and Lunsford, W. F.: Skin Testing for Brucellosis (Undulant Fever) in School Children, Ann. Int. Med. **12**: 495-502, 1938.
4. Evans, A. C.: Studies on Chronic Brucellosis: IV. An Evaluation of the Diagnostic Laboratory Tests, Pub. Health Rep. **53**: 1507-1523, 1938.
5. Huddleson, I. F.: Brucellosis in Man and Animals, ed. 2, New York, Commonwealth Fund, 1943.

time infection has lasted several weeks, but occasionally only after many months, certain "preparatory" changes take place in the endothelium of capillaries in the skin. (Similar allergic changes doubtless occur in other tissues as a result of alteration by, or combination with, brucella protein.) Injection thereafter of homologous protein outside the endothelial wall is followed by inflammatory changes: capillary dilatation, edema and redness, together with varying degrees of general reaction. This happens only provided homologous bacterial protein is still circulating inside these capillary walls. The patient's skin is the test tube in which conjunction of protein takes place. Thus a positive reaction signifies the continued presence of bacterial derivatives in the body regardless of whether they have or will produce recognizable symptoms. A negative test means simply skin anergy, or that no bacterial derivatives remain. Such properties of bacteria were studied by Hanger [6] and Shwartzman [7] almost simultaneously, and the "specific bacterial skin effect" observed became known as the Shwartzman phenomenon. There are of course certain quantitative limits within which the reaction is visible short of skin necrosis. As for time limits and preparatory factors it is necessary that active infection be established. The maximum reaction is reached at forty-eight hours. The class of proteins comprising animal and food allergens behaves quite differently.

Brucellergen (Huddleson,[5] p. 244) is standardized on rabbits after thirty days following inoculation with live cultures. This material for skin testing is an improvement over the earlier use of bacterial filtrates and cell suspensions. These were mixed proteins. Brucellergen is a protein nucleate solution, the test dose being 0.00075 mg. in 0.1 cc. This is 625 times the quantity of mixed protein contained in 2,000,000 brucella cells, a number used previously for skin tests. Severe skin reactions are obviated by the use of nucleoprotein. Sensitivity is moreover so high as to permit detection of at least 95 per cent of chronic cases. Thus false negatives are only 5 per cent at most, except in early cases. False positives, on the other hand, are reduced to zero and specificity is 100 per cent, since the single nucleoprotein does not react with products of common bacterial cells other than brucella. Actually it is possible to go a step further in interpreting a positive reaction than to conclude merely that brucella endotoxin is circulating. Gay [8] states that many bacterial endotoxins are incapable of giving rise to neutralizing antibodies but may give rise to antibodies reacting with the nucleoprotein. In a small trial series precipitin reactions between serum of skin positives and brucellergen were obtained by us in a dilution of the latter as high as 1 : 6,400. Skin negatives did not react. Thus the positive skin test could mean a conjunction of nucleoprotein and antiendotoxin. This explanation as a working hypothesis would satisfy every clinical situation, especially the positive test in the asymptomatic, not to mention the decreasingly intense positives in the treated patient who is recovering. The necessity of active infection as a prerequisite to the establishment of skin sensitivity rules out the one other possibility that the patient merely has been swallowing endotoxin in pasteurized milk. Data on the unimportance of swallowed dead brucella in symptom formation will be published later.

6. Hanger, F. M.: Proc. Soc. Exper. Biol. & Med. **25**: 230, 1927.
7. Shwartzman, G.: Proc. Soc. Exper. Biol. & Med. **25**: 560, 1928; **26**: 207, 1928-1929.
8. Gay, F. P.: Agents of Disease and Host Resistance, Springfield, Ill., Charles C Thomas, publisher, 1935, pp. 67-68.

The significance of a positive brucellergen skin test has been compared to that of a positive tuberculin test. This has led to misunderstanding, since so many of the latter positives have been shown to be inactive cases. The two diseases should be contrasted rather than compared. Most important, it should be remembered that in either case the practical conclusion immediately on reading a positive is to assume that the patient has an active infection until proved otherwise. Only a careful study of either patient will finally determine whether infection is subsiding or is still active. Repeated skin tests in brucellosis after a waiting period may be used when there is doubt. The characteristic symptom complex rather than x-ray or physical findings must be relied on.

The clinical picture of chronic brucellosis or the walking patient has been adequately described in monographs [9] and in the recent reviews of Manchester,[10] Griggs [11] and many others. Perhaps the description of Evans [12] was most succinct when she compared it to "neurasthenia." She challenged the right of application of this label, and by inference that of psychoneurosis, unless chronic brucellosis was first ruled out. Since undulate they will, the symptoms are usually variable in that they alternate with well periods. In psychoneurosis actually there is a great deal more consistency. There is no fever. The aching seems to the observer to be vague, unrelated to organs or to gross anatomy. Physical examinations are negative and blood findings normal. X-ray studies are without objective architectural changes. The physician's credulity is often taxed to the point of annoyance. He becomes tempted to explain peculiar functional derangements by a term which is not synonymous with functional, namely "psychogenic." The very nature of the toxemia in this infection contributes to an invalidism, which, combined with the feeling of frustration in the years spent trying to regain health, does convey the impression of primary psychoneurosis. To differentiate conversion formation from organic reaction, psychiatric consultation is not always readily available. The busy practitioner should therefore welcome such a dependable procedure as the simple skin test. Its application may become as routine as the Kahn in the future; certainly it is indicated in any case of fatigability with muscle pains, bizarre nervousness or atypical dyspepsia.

Although no attempt will be made to discuss other forms of treatment, any method should take into account the peculiar properties of the bacterial cell involved. Brucella cultures differentiate into various rough, smooth, mucoid, virulent and nonvirulent forms. Some have a thin capsule and some have no demonstrable capsule.[13] The only consistent feature of brucella is the extraordinary versatility or adaptability of the microorganism to growth in animal tissues. For the most part the tissue changes produced are reversible, symptoms being on a chemical rather than structural basis. The pathology of brucellosis is well established, but that small foci of active infection may remain undetected during life in spleen, gallbladder, liver or lymph node seems plausible enough to be assumed in a given case.

9. Harris, H. J.: Brucellosis (Undulant Fever): Clinical and Subclinical, New York, Paul B. Hoeber, Inc., 1941. Huddleson.[5]
10. Manchester, R. C.: The Clinical Manifestations and Diagnosis of Chronic Brucellosis, Ann. Int. Med. **16**: 950-965, 1942.
11. Griggs, J. F.: Chronic Brucellosis: Diagnostic Points Noted in 100 Cases, California & West. Med. **58**: 118-124, 1943.
12. Evans, Alice C.: Chronic Brucellosis, J. A. M. A. **103**: 665-667 (Sept. 1) 1934.
13. Huddleson, I. F.: Studies in Brucellosis: I. The Presence of a Capsule on Brucella Cells, Technical Bulletin 117, Michigan State College, 1941, pp. 11-14.

If these foci are found, surgical removal would be the treatment of choice. If not found, medical management remains.

The antigen responsible for producing immunity in animals is extremely labile, being affected both by heat and by chemicals. Only the unaltered living organism produces immunity on vaccination, although Huddleson [14] has succeeded in protecting guinea pigs with a ground cell suspension in which the labile material persists. The 40,000 calves mentioned were given the attentuated culture known as strain No. 19. As yet there is not available for human use a vaccine whose toxicity is decreased and whose antigenic qualities are unmodified or enhanced. The injection of billions of heat killed cells (bacterins) has nothing to commend it in theory or in practice.

Brucellin, as prepared by Huddleson,[15] is a culture filtrate without bacterial cells. Reports of its use are not numerous, especially in a series of ambulatory cases. Used in Malta, in a controlled series of acute forms, it shortened the duration of infection considerably in 82 per cent of cases. Whereas old tuberculin is a glycerin broth, brucellin is a beef liver infusion on which virulent smooth strains of melitensis, suis and abortus have grown for three months. After filtration and sterility tests, 0.5 per cent phenol is added. It contains no endotoxin. After administration in the infected, the "negative phase" with exaggeration of all symptoms is but temporary. The active principle or antigen in such a protein mixture by its very nature defies more exact chemical description but seems to be a nucleoprotein (not identical with brucellergen). At any rate immune response is encouraged, since there is elevation of temperature and perhaps a creation of (neutralizing ?) antibodies.

TABLE 1.—*Results of 1,065 Skin Tests*

Total past or present infection	146
Positive skin test	141 (13.2%)
Negative skin, positive agglutination	5 (3.4%)
Treated with brucellin alone	97
Brucellin plus x-ray radiation	4
Heat killed vaccine	5
Refused treatment	4
Not treated	36 (25%)

CLINICAL MATERIAL

The brucellergin skin test has been performed on over 1,800 clinic and hospital patients during the past two years, until it has become an almost routine procedure. Results of the first 1,065 tests done between March 6, 1943 and Dec. 6, 1944 are given in table 1. No skin necroses were produced even with the full dosage, although several showed intense vesiculation. Of the original group of 146 cases in which the diagnosis of past or present infection was made, no specific treatment was given in 36, or 25 per cent. It is probable that several of these should have been treated, in the light of present knowledge. Seven persons who returned one year later and who had a second positive skin test are included in the first series of 97 treated. Only a small fraction of positives are not given specific treatment at this time, a few of course having as serious a coincident pathologic condition as carcinoma for contraindication.

A detailed clinical history was taken and physical examination with tentative diagnosis was made on admission. All laboratory and x-ray studies then proceeded while the result of the skin test was being awaited. Effort to elicit definite history of raw milk consumption or contact with infected herds was met with success a few times, but denial of exposure obviously had no value. All occupations were represented. Sexes were almost equal. Ages were predominantly in the forties. One, a boy of 13, had a seven year history and previous ineffective treatment with bacterins. Several persons were past 65. Average duration of symptoms, excluding 1 case of three months and 1 of twenty-eight years, was slightly over three years. Chief complaints were as reported by others: (1) fatigability, (2) aches and pains, (3) nervousness and (4) indigestion, dyspepsia, bilious spells, bloating and constipation. Abnormal fatigue was invariably listed in every history, but one of the other symptoms often held sufficient prominence to be mentioned first.

THE SANSUM CLINIC
SCHEDULE AND RECORD
for BRUCELLIN Injections

Name.....

No.	Date:	Dose:	Route:	Reactions..... Fever ?
1	.....	0.05 cc. or .... cc.	intradermal	.....
2	.....	0.10 cc. or .... cc.	subcutaneous	.....
3	.....	0.15 cc. or .... cc.	subcutaneous or intramuscular	.....
4	.....	0.20 cc. or .... cc.	subcutaneous or intramuscular	.....
5	.....	0.25 cc. or .... cc.	subcutaneous or intramuscular	.....

A report to the doctor by letter or phone is suggested here.

6	.....	0.30 cc. or .... cc.		.....
7	.....	0.35 cc. or .... cc.		.....
8	.....	0.40 cc. or .... cc.		.....
9	.....	0.45 cc. or .... cc.		.....
10	.....	0.50 cc. or .... cc.		.....

Reactions expected are chills, temperature rise of 2 to 4 degrees with exaggerations of symptoms as aching, indigestion or constipation, these subsiding in one to three days.

Liberal use of aspirin, fruit juices and light carbohydrate midmeal feedings suggested.

As the number of injections increase the degree of systemic reactions decreases until at the end of eight to fifteen injections there is almost no reaction except local redness. A rest period of two months may be taken then, a second course with the first small injections of 0.1 cc. or less being repeated if symptoms have again arisen.

Skin test to determine the presence of circulating endotoxin antigen by means of nucleoprotein, "brucellergen," may be done two, three or six months after the final injection.

.....M.D.

Date.....194.....

Afternoon admission temperatures were usually normal or slightly subnormal but in one third of the cases were between 99.2 and 99.8 F. In a single instance of daily fever for three years the temperature was 100 F. This patient was skin negative, but there was positive serum agglutination in a dilution of 1:320. She became skin positive six months after treatment began, the degree of reaction declining in subsequent tests after improvement. Weight was normal in half the cases, below normal 10 to 20 pounds in one fourth and above normal in the remainder.

Physical examinations were without objective findings except the occasional mention of reddened eyelids or sallow complexion. Attempts to palpate enlargement of the spleen met with success in but 2 cases. Sedimentation rates were usually normal. Basal rates were usually slightly below normal. Blood tests for agglutination were kept at a minimum to avoid taxing available laboratory facilities. In a group of 75 patients the agglutination was positive in only 24, or 32 per cent, and the titer only 1:25 in 4 of these. Thus the percentage of frank positives was only 26. Blood culture done on

14. Huddleson, I. F.: Studies in Brucellosis: II. The Immunization of Guinea Pigs Against Brucella Infection, Technical Bulletin 182, Michigan State College, 1943, pp. 45-56.
15. Huddleson: Brucellosis in Man and Animals, pp. 141, 154 and 162.

a number of occasions was invariably negative. Opsonophagocytic indexes were omitted as too time consuming if not actually superfluous.

Since many patients did not reside in the city, these were supplied with brucellin and given a printed schedule of suggested dosage for the physician's use at home. Seventeen persons received all injections at the clinic. The initial dose was 0.05 to 0.1 cc., depending on the severity of the skin test reaction, and this initial dose given intradermally determined the patient's reactive ability. Very rarely was it necessary to dilute the brucellin. The patient was warned that he might expect a chill, fever, and an exaggeration of his symptoms. This appeared in eight to twelve hours after a subcutaneous and within four hours after an intramuscular injection. Reaction symptoms subsided in two or three days and decreased in severity as the number of injections increased. When almost no systemic reaction was obtained after a series of perhaps ten to twelve weekly injections a rest period was advised. The level of immunity so obtained was sufficient to neutralize subsequent, now milder, attacks, but repeated courses of brucellin were given if symptoms recurred instead of decreasing. One course would last two to six months, after which subsequent skin tests were performed when possible, a positive test being followed by additional injections if symptoms persisted.

REPORT OF CASES

CASE 1.—B. L., a man aged 43, a dock foreman, whose weight was 235 pounds (117 Kg.) and height 75 inches (191 cm.), was admitted to the Sansum Clinic Aug. 10, 1943 with the chief complaint of tiredness for three years. Several days at a time he would feel quite well but suddenly again would feel "terrible." He explained each attack of abdominal pain or soreness as if the food did not digest but stopped in the stomach, causing bloating and constipation. During attacks he became irritable, short tempered and worried over minor problems. Three years previously he had had "flu" most of one winter, with congestion in his chest, and he said he "could hardly drag around" at night. Six months afterward there appeared a mild degree of jaundice without pain but with extreme fatigue. Muscular effort later began to be followed by chills and then fever. There had been occasional dry hacking cough since the jaundice, recurrent constipation, occasional difficulty in starting the urinary stream and a decline in sexual potency. The generalized urticaria of recent months was slightly relieved, he thought, by following advice to omit all milk. He had consumed raw milk by preference, obtained from a large metropolitan dairy three years previously and to a lesser extent since.

The admission afternoon temperature was 98.6 F. Physical examination revealed that the patient was well built with a few scattered large urticarial wheals on the skin, slightly reddened eyelids and dry lips. There was slight tenderness over the gallbladder, cecum and transverse colon. The abdominal reflexes were absent. His blood pressure was 150/88.

Blood count was 5,380,000 red cells, 17 Gm. or 108 per cent hemoglobin and 6,900 white cells with 63 per cent polymorphonuclears. The icterus index was 10.5, the Kahn reaction negative, brucella agglutination positive in a 1:50 dilution. Fasting blood sugar and four hour oral glucose tolerance readings were 82, 102, 106, 96 and 72 mg. per hundred cubic centimeters respectively. Urinalysis was normal. An Ewald test meal showed free acid of 25 degrees with a total acid of 30 degrees. Gallbladder studies after Priodex orally showed excellent filling with the dye, only 30 per cent emptying, and three small opaque stones 3 mm. in diameter in the fundus. Only 0.08 cc. of brucellergen was used for the skin test. The reaction was 5 plus in forty-eight hours with general reaction and a wheal measuring 5 by 10 cm.

Brucellin was given every two weeks by us in the clinic. The first injection of 0.05 cc., intradermally, was followed in ten hours by a chill and a temperature of 102 F. Next morning it was 99.8 F., rising in the evening to 101 F. Although headache and prostration were severe the patient was feeling much better by the fourth day. After the second injection of 0.1 cc. subcutaneously there was a chill, rise in temperature to 101 F. by morning and 103 F. by evening and then a drenching sweat. He was unable to work for five days. His eyes were red and swollen; of all symptoms the indigestion and the urticaria were the most severe. The second week he improved. Reactions gradually became less troublesome; urticaria disappeared. To the tenth injection of 0.6 cc. there was no reaction. Three weeks later, Dec. 26, 1943, he appeared for examination stating that he "felt like a million dollars." He had declined a gallbladder operation. Nine months after recovery he was still working and had no complaints. At eleven months there occurred an attack of indigestion again. Dec. 26, 1944 a skin test was 3 plus, without general reaction. He immediately began a course of brucellin, reacting only to the first dose in a series of five injections. He then had a cholecystectomy performed by his family physician, Dr. Walter Boyd of Long Beach, Calif., March 18, 1945. He made a rapid recovery from the operation.

The foregoing could be called the textbook description of chronic brucellosis with a full recital of symptoms referable to all tissues. Treatment reactions are typical. It also illustrates probably the most common route of invasion (jejunal mucosa, lacteals, liver) and focal point for persistence of infection. This focus can be held almost completely in abeyance for many months only to light up again suddenly.

CASE 2.—J. T., a man aged 54, a salesman, whose weight was 173 pounds (78.5 Kg.) and height 66 inches (168 cm.) was admitted to the clinic Sept. 1, 1943 complaining of burning pain in the chest for one year. Onset was gradual with heartburn and stomachache, worse since a severe head cold three months before. The pain, which was now unremitting, was localized just to the right of the sternum. He was unable to walk a block without feeling so weak as to be able barely to stand; he had become slightly yellow he thought; he did not perspire; his heart pounded on exertion. He had drunk goat's milk three months previously at a neighbor's suggestion but recalled having not felt well for at least two years.

On admission the temperature was 98.6 F. Physical examination revealed that the patient was overweight, not dyspneic but looking chronically ill. The skin was dry and pale, with numerous small patches of psoriasis. The heart tones were of only fair quality; there were no murmurs; the rate was 104, regular. There was very slight tenderness over the gallbladder. The blood count was 6,250,000 red cells, hemoglobin 16.5 Gm. or 103 per cent, and 11,100 white cells with 64 per cent polymorphonuclears. The Kahn reaction was negative. The fasting blood sugar was 136 mg., the blood uric acid 1.9 mg. and serum cholesterol 310 mg. per hundred cubic centimeters. An electrocardiogram showed a deep Q_3 equal to R_3 with T_3 sharply inverted. The brucellergen skin test was 4 plus. Agglutination was negative, December 20.

He was placed on a reducing diet without insulin, aminophylline 3 grains (0.2 Gm.) every four hours and brucellin every two weeks. Little reaction and no relief of pain followed the first few doses, but to the seventh injection of 0.45 cc. the response was a temperature of 103 F. During this time he developed a generalized eczematous dermatitis, but the constant chest pain gradually disappeared. Feb. 1, 1944, four months after treatment began, he stated that he was "100 per cent well." He resumed traveling. He received three courses of brucellin, twelve, six and four doses. Each course followed a skin test progressively less positive. Fourteen months after admission the skin test was entirely negative. Three subsequent electrocardiograms made Dec. 20, 1943, Aug. 14, 1944 and Feb. 23, 1945 were essentially the same as on admission, with minor temporary improvements in Q_3 and T_3, but the patient appeared well, had no pain, and felt no fatigue. The dermatitis disappeared slowly but completely.

This patient still has coronary disease and he has been advised to regulate his life accordingly. The added burden of infection has apparently been removed.

CASE 3.—J. B., a woman aged 52, a housewife, was first admitted to the Cottage Hospital Oct. 31, 1930, at which time she complained of attacks of stomach trouble, constipation, nervousness, headaches, dizziness and palpitation of one year's duration. Alternating with well periods these "bilious attacks" produced epigastric pain together with exaggeration of many other complaints, including a feeling of pins and needles in the extremities. Physical and laboratory examinations at that time were not remarkable, and complete x-ray studies of the gallbladder and gastrointestinal tract were negative. Temperature readings above normal on four occasions during thirty days' hospitalization were only 99.2, 99.4, 99.6 and 99.8 F. The second admission nearly fourteen years later was June 15, 1944. There were exactly the same complaints with emphasis on constipation and insomnia, and they were almost continuous. Her constant fretting in the hospital now made life miserable for the nurses, who tolerated her spoiled child attitudes only because they also knew she wept for her only son as a prisoner on Bataan. She had little desire for food but was only 7 pounds (3.2 Kg.) underweight, as compared to 15 pounds (6.8 Kg.) on the previous admission. Gallbladder, stomach, small bowel, and colon x-ray studies were again negative. The brucellergen skin test June 20, 1944 was 2 plus in twenty-four hours and 4 plus at forty-eight hours, with a slight general reaction. Agglutination was negative.

TABLE 2.—*Results of Brucellin Treatment*

	Number	Per Cent
Unimproved	8	10.3
Moderately improved	22	28.2
Greatly improved	48	61.5
Total	78	100.0

To the first dose of brucellin, 0.1 cc., she reacted with a temperature of 100.4 F. Headache was increased. One week later she was sleeping better and seemed cheerful. She was discharged June 29, 1944, and the injections were given at home by her physician. She telephoned every week and returned on two occasions to report that the injections, nine in all, produced decreasing reactions and that she felt perfectly well and took no sedatives or laxatives. She wanted to apologize to the nurses for the way she acted in the hospital. Her cheerfulness amazed and delighted her friends. Ten months later, April 15, 1945, she telephoned to say she was having some aching pain in her legs. She was advised to take a small course of brucellin and reported after the third dose that only the first injection produced any reaction, that she now felt very well and that she had gained 15 pounds since the beginning of treatment.

It is amazing that symptoms should persist for fifteen years without increasing appreciably in severity but only in frequency. There was ample reason for her to appear psychoneurotic. The melancholia, which might have been called involutional, reached even to suicidal notions. The situation is now quite reversed in that she holds up her husband in their grief over the loss of their son.

CASE 4.—E. W., a man aged 65, a butler, entered the Cottage Hospital Oct. 10, 1943 complaining of a swollen right knee for several weeks. He walked with a cane, but there was relatively little actual pain and no tenderness in the one joint area. He weighed 240 pounds (109 Kg.). The temperature was normal. His blood pressure was 156/90. X-ray of the knee was negative, as was a gallbladder study. Blood count was 4,020,000 red cells with 90 per cent hemoglobin, and 9,150 white cells with 63 per cent polymorphonuclears. The sedimentation rate was 6 mm. in one hour. The serum cholesterol was 286 mg., the blood uric acid 3.8 mg. The basal metabolic rate was plus 8. The electrocardiogram showed left axis shift.

Twenty-four hours after the brucellergen skin test the knee was much worse; at forty-eight hours the skin reaction was 4 plus, but he felt better. An Ace bandage was applied to the knee. Brucellin was begun October 28 with a dose of 0.1 cc. He returned in a week believing that the knee would have to be opened on the outer side, where there was increased swelling and a red area measuring about 5 by 10 cm. There was no fluctuation. Brucellin was increased, and after the third injection the strength and flexibility of the knee had improved. He walked without a cane after two more and then received a total of only seven injections, the highest single dose being 0.9 cc.

This shows in a local area what may occur on a larger scale at the origins or the insertions of muscles, explaining in part the muscular weakness and disability so common in this infection.

RESULTS OF TREATMENT

Of the 97 patients treated with brucellin all but 19 have completed at least one course of injections, responded to follow-up inquiry or returned for examination and have gone at least six months without return of symptoms. Results are given in table 2. Three of the eight listed as failures discontinued treatment after five injections. One was unchanged after fifty injections.

Twenty-two of the 78 persons followed, or 28 per cent, were moderately improved. One was diabetic, 1 hypertensive, and 1 a chronic alcoholic addict. If some may have broken off treatment too soon because of early severe and unpleasant systemic reactions, others probably reacted too mildly to insure the production of higher immunity. All in this group were, as the adjective implies, improved in definite measure but without achieving the enthusiasm or self assurance of improvement shared by the next group. Search for hidden persistent foci perhaps should be most diligently made in the moderately improved case, and even more simplified easily controlled means of therapy welcomed.

Forty-eight of the 78 persons treated, or 61 per cent, were greatly improved. This included 6 whose skin tests after treatment and a waiting period were negative and might be listed as "cured." Most of these patients reacted violently to early injections and made an immediate improvement, which steadily increased until such a time as there was no longer any doubt in their own minds that they were well. Recurrences in this group might not be expected until several months had elapsed, but only by a plan of constant checkup of skin reaction could this be controlled. Such a plan is being followed.

COMMENT

Nearly as many additional cases as in this first series are being treated at this time. Results are substantially the same. Irradiation of abdominal lymph nodes or the spleen has been done in those cases whose level of immunity does not rise rapidly as evidenced by weak febrile response to early injections of brucellin or to later "booster" doses. A report of the results in these cases will appear later. Data are being accumulated from findings at exploratory operation for coincident pathologic conditions which may throw some light on the location and size of focal areas of chronic infection. So far the evidence of visible and palpable pathologic change is so meager as to inculpate the spleen, whose smooth surface may conceal small abscesses within, as much as the gallbladder, which may carry the organism in its reservoir. Possibly splenectomy should be contemplated as often as cholecystectomy.

Exactly how brucellin works and of what immunity in brucellosis consists cannot yet be stated with cer-

tainty. As a protein solution it doubtless gives rise to certain antibodies. The procedure is not a matter simply of desensitization. The hypothesis that brucellin antibodies neutralize endotoxin and hold in check the growth of brucella is at least practical in that it describes the changes taking place in the improved case. This improvement is sufficiently rapid in a high enough percentage of cases to serve as another aid in the diagnosis of the cause of elusive, enigmatic symptoms, which, however real to the patient, may otherwise be only a riddle to the most careful consultant. Complete cure finally may have to wait on additional even untried methods of treatment.

SUMMARY AND CONCLUSIONS

1. Brucellosis is one of the most prevalent of modern diseases.

2. The intradermal skin test is the most reliable means of confirming the clinical diagnosis of chronic brucellosis.

3. Of 1,065 persons tested, 13.2 per cent showed a positive reaction to brucella nucleoprotein.

4. Seventy-five per cent of all positives in this series were considered to have persistent infection and were actively treated.

5. Of 97 cases treated with "brucellin," 78 were followed adequately, with 70 cases improved and 8 unimproved.

6. The skin test should be repeated every six months with the expectation that only a negative reaction denotes a cure.

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RANGE OF BLOOD PRESSURE IN HYPERTENSION

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The variability of the blood pressure poses numerous problems in the evaluation of subjects with hypertension. Thus, in estimating prognosis and the response to treatment, and in examining candidates for military service or insurance, it is well recognized that casual readings of the blood pressure may be misleading. Numerous reports have called attention to the lability of the blood pressure in hypertensive subjects.[1] It is our purpose in this report to emphasize the desirability of recording the blood pressure, particularly in hypertensive subjects, in terms of maximum and minimum range rather than as an individual reading, and to suggest a simple procedure whereby this may be accomplished.

As mentioned in a previous report in THE JOURNAL,[2] various pressor and depressor agents have been employed to study blood pressure responses in normal persons and in hypertension. The rise in blood pressure has been investigated following tyramine, epinephrine, pitressin, tobacco smoking, physical work, painful and irritant stimuli, exercise of muscles with circulation arrested, prostatic massage, immersion of the hands in cold water, anoxemia, inhalation of carbon dioxide and breath holding.[3] Methods employed to provoke a fall in blood pressure include oral barbiturates such as barbital, and sodium amytal, intravenous pentothal, hyperventilation, carotid sinus pressure, histamine, acetyl-beta-methylcholine, amyl nitrite, sodium nitrite, spinal anesthesia and bed rest for a period of twenty-four hours with observations during sleep.[4]

Most of these procedures are not well suited for routine clinical use. The cold pressor test has been widely employed to detect a "prehypertensive state," an exaggerated rise above the initial level supposedly indicating a constitutional predisposition to hypertension.[5] The validity of this interpretation has been questioned,[6] but pressor tests are useful as a measure of a person's "ceiling" blood pressure level. The simplest of the pressor tests is breath holding, and of the depressor procedures hyperventilation and carotid sinus pressure. Whereas breath holding raises the blood pressure, hyperventilation causes a fall.[7] Pressure on the carotid sinus likewise decreases the level of the blood pressure, particularly in hypertensive subjects.[8] A study was carried out in 30 cases of essential hypertension to determine the practical utility of these tests.

In each case the pressor effect of breath holding was compared with the cold pressor test; and the depressor response to hyperventilation, pressure above the carotid sinus and combined hyperventilation plus carotid pressure was compared with the effect of 9 grains (0.6 Gm.) of sodium amytal given hourly in 3 grain (0.2 Gm.) doses as recommended by Allen and Adson.[9] Comparison was made also with the maximum and minimum arterial pressures recorded during the period of hospitalization. In 18 cases, including 13 from the aforementioned series, further investigation was made of the pressor response to brief inhalation of aromatic spirit of ammonia compared to the breath holding pressor response.

The technic employed in the breath holding and hyperventilation tests was as follows: At the end of a normal expiration the subject was instructed to stop breathing without straining. After twenty seconds of apnea the highest systolic pressure was recorded. The subject was then permitted to breathe normally for a few moments and the test was again repeated, this time

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(Footnotes continued on next page)

the highest diastolic level being recorded after twenty seconds of apnea. Most persons find it difficult to refrain from breathing for more than thirty seconds when respiration is suspended in expiration, and because of the rapid changes in blood pressure it is preferable to observe the systolic and diastolic rise on separate tests. Because of the difficulty some persons, particularly older subjects, experience in maintaining apnea for sufficient time to record blood pressure changes, an additional simple pressor test was employed. A piece of gauze saturated with aromatic spirit of ammonia was held over the nose, and the blood pressure was determined during brief inhalations of this irritant. This test has an advantage over the breath holding test in that it does not require cooperation, and the pressor response is not so transient as with the breath holding test, so that the rise in blood pressure may be more accurately recorded.

TABLE 1.—*Average Blood Pressure Responses in Thirty Cases of Essential Hypertension*

Routine Readings During Hospitalization	Initial Reading	High	Low	Change from Initial Reading: Systolic	Change from Initial Reading: Diastolic
		208/124	174/104		
Breath holding	181/110	208/133	.....	+27	+23
Cold pressor test	187/112	211/130	.....	+24	+18
Hyperventilation	187/114	.....	171/103	−16	−11
Carotid pressure	190/116	.....	169/101	−21	−15
Hyperventilation plus carotid pressure	187/113	.....	157/ 94	−30	−19
Sodium amytal	189/114	.....	151/ 97	−38	−17

After performing the pressor test the subject was instructed to breathe maximally with deep inhalations and exhalations at a slightly rapid rate without effort or straining. The blood pressure was recorded after thirty to sixty seconds of hyperventilation. With the patient still breathing deeply, digital pressure was applied over the carotid sinus, preferably the left, and the lowest blood pressure attained during the next half minute was recorded. The patient should be apprised as to the nature of the carotid pressure test before it is carried out, so that a psychic reaction to neck pressure is avoided. The depressor response following carotid sinus pressure occasionally persists for several minutes, and therefore the pressor response should be tested first. The maximum and minimum levels attained during the pressor and depressor tests are recorded, e. g. as 208/133-157/94. Because of occasional significant differences in blood pressure in the two arms,[10] all readings should be made in the same arm, preferably the right arm. Diastolic readings as here reported are recorded at the fourth phase. The entire test occupies less than five minutes and no preparation is necessary.

The findings in the series of 30 cases studied are summarized in table 1, together with the highest and lowest routine readings during hospitalization and the response to the cold pressor and sodium amytal tests.

The average maximum blood pressure levels attained with the breath holding and with the cold pressor tests were similar (breath holding 208/133, cold pressor 211/130) and correspond closely to the highest blood pressure recorded routinely during the period of hospitalization (208/124). Most frequently the admission blood pressure was highest; indeed, the initial blood pressure reading on physical examination may be regarded as a psychic pressor test and has been recognized as having the same significance. In 18 cases the pressor effect of ammonia inhalation and of breath holding was compared (table 2). The rise in diastolic pressure was similar (ammonia 24 mm., apnea 22 mm.) but the increase in systolic pressure was distinctly greater with ammonia inhalation (ammonia 37 mm., apnea 27 mm.). Stimulation of the trigeminal nerve by ammonia inhalation, as Allen [11] has shown experimentally, not only provokes a decided rise in blood pressure but causes involuntary suppression of respiration. The striking pressor effect observed with ammonia inhalation may therefore in part be due to apnea in addition to trigeminal stimulation. In normal persons, as shown by Bing,[12] inhalation of irritants such as acetic acid or ammonia ordinarily raises the blood pressure approximately 10 mm., only exceptionally as much as 20 to 25 mm.

Hyperventilation alone reduced the blood pressure from 187/114 to 171/103. Carotid pressure alone caused a fall from 190/116 to 169/101. The effect of hyperventilation combined with carotid pressure was distinctly greater than with either procedure alone, the blood pressure falling from 187/113 to 157/94. These findings correspond fairly closely to the results obtained with 9 Gm. of sodium amytal, in which the blood pressure fell from 189/114 to 151/97. With hyperventilation plus carotid pressure the average fall in systolic pressure was 30 mm. compared with 38 mm. with sodium amytal. The fall in diastolic pressure was

TABLE 2.—*Pressor Effect of Ammonia Inhalation and Breath Holding (Eighteen Cases)*

	Initial Reading	Final Reading	Change: Systolic	Change: Diastolic
Ammonia	176/104	213/128	+37	+24
Breath holding	175/104	202/126	+27	+22
Hyperventilation plus carotid sinus pressure	181/105	146/ 87	−35	−18

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slightly greater with hyperventilation plus carotid pressure (19 mm.) than with sodium amytal (17 mm.).

The greater fall in systolic pressure obtained with sodium amytal may be attributed in part to a decrease in cardiac output. Blood pressure is influenced not only by vasomotor control of the arterioles but also by systolic cardiac output and the heart rate. While in certain individuals carotid sinus pressure causes a definite sinus bradycardia, this factor did not contribute significantly to the depressor effect in the cases studied. When pressure is exerted on the left rather than on the right carotid sinus, slowing of the heart rate is negligible although the depressor response is equally great. In 2 subjects in whom definite bradycardia developed on carotid sinus pressure, intravenous administration of atropine 1/50 grain (0.0013 Gm.) prevented slowing of the heart rate but did not inhibit the fall in blood pressure. Mandelstamm and Lifschitz [13] likewise found in an extensive study that the depressor effect of left and right carotid sinus pressure was the same and that administration of atropine prevented slowing of the heart rate but did not influence the fall in blood pressure. Similar observations were made by Galdston and his associates,[14] who noted further that following administration of atropine the fall in arterial pressure on carotid sinus stimulation was in fact often greater than before its injection. The depressor effect of overventilation is not due to the mechanical effect of respiration on the circulation, for no fall in blood pressure occurs if hyperventilation is carried out with air containing carbon dioxide.[3] As shown by Dale and Evans,[15] carbon dioxide is necessary for the normal functioning of the vasoconstrictor center, and the blood pressure changes with apnea and overventilation are to be attributed to the specific effect of carbon dioxide on the vasomotor center.

COMMENT

In a recent review of normal blood pressure and its variations by Allen [16] it was emphasized that "a single measurement of blood pressure, especially in a person who is anxious or emotionally unstable, can have little value. . . . The only way in which to learn all the facts about blood pressure is to make readings at frequent intervals during the day and night, and daily over a period of at least a week." Employment of the procedures suggested in this study, i. e. blood pressure determination during breath holding or inhalation of spirit of ammonia and during hyperventilation plus carotid pressure, makes it possible to obtain information concerning the range of blood pressure in much simpler fashion. These tests may be carried out with little more time or effort than is required to record the blood pressure on routine examination. The breath holding and ammonia blood pressure levels are as high as or higher than the cold pressor "ceiling." Conversely the depressor effect of hyperventilation plus carotid pressure is similar to that of sodium amytal, which has been regarded as the best of the depressor tests.[17]

Pressor, and particularly depressor, tests are of value not only in estimating the status of the hypertensive subject but also in the selection of therapeutic measures. Thus, Allen and Adson [18] find that "the more nearly the blood pressure approaches normal as a result of rest, administration of sodium amytal and the injection of pentothal, and the less marked the vascular disease the more likely extensive sympathectomy is to reduce the blood pressure significantly. . . . When blood pressure is not reduced markedly it is useless to perform extensive sympathectomy for essential hypertension."

The procedures employed to study blood pressure responses, i. e. hyperventilation, pressure above the carotid sinus, administration of barbiturates, spinal anesthesia and observation of blood pressure on prolonged bed rest and during sleep, all operate by decreasing vasomotor tone and give the basal blood pressure relatively free of the influence of the vasomotor center. Conversely, pressor tests such as immersion of the hand in cold water, inhalation of carbon dioxide and breath holding accentuate vasomotor activity by stimulating the vasomotor center. It becomes possible, therefore, employing the breath holding pressor test and the hyperventilation-carotid pressure depressor test to differentiate the vasomotor or neurogenic component in hypertension from the humoral factor, whose maximal effect presumably is indicated by the basal blood pressure free from vasomotor influence.

In renal hypertension the blood pressure is relatively fixed and is but slightly influenced by pressor and depressor procedures, in contrast to essential hypertension.[19] These findings in renal hypertension indicate that the basal blood pressure is set at a high level by the humoral renal pressor mechanism and that the vasomotor or neurogenic component is relatively negligible. It is of interest that in essential hypertension, unlike renal hypertension, the blood pressure falls to a much greater degree with depressor tests. A spontaneous fall in blood pressure to normal occurs very frequently in essential hypertension. Fifty-six per cent of 76 unselected, untreated cases studied by Ayman exhibited this finding.[20]

An average diastolic pressure of 91 was attained with hyperventilation plus carotid pressure in the 35 cases studied. This is but slightly above normal limits. In fully 20 of the total of 35 subjects in whom pressor and depressor responses were investigated, the minimum blood pressure fell to well within the normal range. In these 20 subjects with an average maximal blood pressure of 203/118 the minimum pressure on depressor testing average 122/75. The attainment of normal blood pressure in the majority of cases by inhibition of vasomotor control suggests inescapably that, in the earlier stages of essential hypertension at least, the humoral factor does not play an important role and that the neurogenic or vasomotor component is the more important determinant in the elevation of blood pressure.

Vasomotor control of arteriolar tonus is exerted chiefly in the splanchnic area. The observations of Jansen, Tams and Achelis [21] indicated that the vasoconstriction producing hypertension is confined chiefly to the splanchnic area. This concept, questioned by

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some,[22] has been sustained by the more recent studies of Eichna and Wilkins, Abramson and Fierst, Sheard and his associates and Apperly and Cary.[23] These investigators have demonstrated an unequal distribution of blood flow in hypertension with augmented circulation to the extremities, signifying splanchnic vasoconstriction. As pointed out by Abramson,[24] these observations weaken the hypothesis that hypertension is due to a humoral vasoconstrictor substance, for under such circumstances generalized arteriolar vasoconstriction would be expected to occur, involving the extremities as well as the remainder of the vascular bed.

Further evidence that vasoconstriction is limited chiefly to the splanchnic area in hypertension is afforded by the distribution of sclerosis in the arterioles. Arteriolosclerosis, which follows prolonged vasoconstriction in hypertension,[25] occurs preponderantly in the abdominal viscera, i. e. the kidney, spleen, pancreas and liver.[26] The terminal arterioles of the other organs, excepting the brain, are rarely involved in the arteriolosclerotic process and then to only an insignificant extent.

The regular findings of arteriolosclerosis in the kidneys of hypertensive subjects at necropsy suggested, after Goldblatt's demonstration that renal ischemia could produce hypertension experimentally,[27] that renal ischemia might also be the basis of human hypertension.

It has been shown by Page and his co-workers [28] and by Braun-Menendez and his associates [29] that the kidney liberates a proteolytic enzyme (renin) into the blood stream which acts on one of the blood globulins (a_2 globulin) to produce a polypeptide with a pressor effect (angiotonin, hypertensin). An increase in circulating renin and angiotonin has been reported in experimental renal ischemia [30] and clinically in eclampsia and severe glomerulonephritis.[31] Another pressor mechanism has been demonstrated in the ischemic kidney, i. e. the production of pressor amines by decarboxylation of certain aromatic amino acids.[32] In the presence of adequate oxygen such pressor amines are converted to inactive aldehydes by renal amine oxidases.

There is no evidence, however, that either the renin or the pressor amine mechanism is the cause of human hypertension. Renin is not found in the blood in essential hypertension [33] (although it is observed in renal hypertension as in severe glomerulonephritis), nor is there an increase of the globulin substrate precursor of angiotonin in essential hypertension.[34] The questionable role of humoral pressor substances in hypertension is suggested further by the failure of extensive transfusions from hypertensive subjects to cause any elevation of blood pressure in the recipients.[35]

If essential hypertension were due to a humoral pressor substance one would expect widespread vasoconstriction of the vascular bed. However, the vasoconstrictor in essential hypertension is limited to the vessels under most active vasomotor control, i. e. the arterioles, and as already mentioned is most striking in the splanchnic bed. In nephritic hypertension, in eclampsia and in malignant nephrosclerosis (hypertension with renal insufficiency), as Fishberg [36] remarks, "there is often a high degree of accompanying capillary and venular constriction, so that the patient appears pale," whereas "in the benign phases of essential hypertension there is relatively little accompanying capillary and venular constriction, for which reason the patient may appear ruddy." This distinction provided the basis for Volhard's classification of hypertension into pale and red types,[37] a concept which is supported by the recent demonstration of circulating pressor substances in renal but not in essential hypertension. The pressor amines cause generalized vasoconstriction,[38] and while the effects of angiotonin more closely resemble those of human essential hypertension, angiotonin causes vasoconstriction of the pulmonary arterioles, whereas this does not occur in human hypertension.[39]

Conclusive evidence that renal ischemia with its attendant pressor effect is not responsible for essential hypertension is afforded by several studies demonstrating that renal blood flow in this condition is normal.[39]

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This is consistent with pathologic studies based on renal biopsy obtained during sympathectomy in which no evidence of renal arteriolosclerosis was found in the earlier stages of essential hypertension.[40] It is evident, therefore, that arteriolosclerosis of the kidneys and renal ischemia cannot be responsible for the genesis of essential hypertension. The role of the kidney in essential hypertension has been thus summarized by Smith and his collaborators:[41] "So far as the genesis of essential hypertension is concerned, the kidney appears to be the victim rather than the culprit." Page[42] expresses a similar view: "The evidence taken as a whole offers little support for the view that persistent reduction of blood flow and oxygen utilization occurs within the kidneys except when hypertension is of long duration and severe secondary vascular change has supervened."

In later stages of essential hypertension renal arteriolosclerosis occurs constantly, with a decrease in renal blood flow paralleling the severity of the vascular changes in the kidneys.[43] With the development of organic lesions in the renal arterioles and decreased renal blood flow in long standing essential hypertension and in malignant hypertension it is likely that the renal pressor factor may come to play a role in hypertension. That a humoral component is important in the later stages of hypertension and particularly in malignant nephrosclerosis is indicated by the failure of depressor agents acting on the vasomotor center, or sympathectomy, to influence beneficially the elevated blood pressure.[18] Page,[42] employing perfusion of the rabbit's ear, has shown that a protein vasoconstrictor substance similar to angiotonin occurs in human serum after a wide variety of renal injury causing hypertension and is regularly present in the malignant phase of essential hypertension. He suggests that determination of this peripheral vasoconstrictor substance gives an indication that the humoral mechanism has come into action.

Consideration of the renal pressor and depressor mechanisms has been concerned chiefly with their significance in hypertension. While these agents do not appear to play a part in the etiology of hypertension, it is possible that they perform an important physiologic function in the normal individual. The blood pressure influencing agents of the kidney may normally function in maintaining the basal "vital" level of the blood pressure. Superimposed on this, a variable control is exercised by the vasomotor center in response to requirements determined by physiologic and environmental changes. The two components may be distinguished by employing the tests already suggested.

Renin is not a pathologic constituent, for it has repeatedly been demonstrated in extracts of renal tissue since Tigerstedt and Bergmann's original experiments in 1898. This proteolytic enzyme apparently is a normal enzyme of renal tissue, i. e., a cathepsin. Under abnormal metabolic conditions in the kidney which are known to produce hypertension (e. g., ischemia due to arterial or venous obstruction, toxic interference with function as in glomerulonephritis, mechanical interference with function as in urinary tract obstruction, functional overloading as in extensive extirpation of renal tissue), the proteolytic enzyme renin may be passed into the circulation in increased amounts, possibly as the result of altered permeability of the renal cells. That an increased loss of normally present renin, rather than an increased production, occurs is suggested by the finding of increased amounts of renin in the circulation in acute experiments, as in renal ischemia produced by hemorrhage or clamping the renal artery.[30]

Increasing doubt that the kidney plays a primary role in the genesis of hypertension focuses attention on other factors as a cause of the heightened vascular reactivity. Conceivably, the increased pressor response to such agents as carbon dioxide and painful (cold) and irritant (ammonia inhalation) stimuli might be due to a local increased sensitivity of the arterioles themselves to pressor stimuli. Fatherree and Brown[44] have shown, however, that there is no essential difference in the sensitivity of the arterioles of normal and hypertensive subjects to the administration of epinephrine, a substance whose vasoconstrictor activity is exerted directly on the arterioles. As stated by these investigators, their study "supports the idea that in hypertension the abnormality which results in an overactivity of the vasomotor system in response to certain stimuli, such as carbon dioxide and cold, is not the result of any hypersensitivity of the arterioles to pressor stimuli but is probably situated centrally in the vasomotor centers." Heightened local arteriolar reactivity to pressor stimuli may, however, be significant in later stages of hypertension, for the hypertrophy of the muscular media which regularly occurs predisposes to exaggerated constriction in response to pressor stimuli. Hypertrophy of the muscular media, once initiated, may explain the frequent persistence of elevated blood pressure after removal of an atrophic or pyelonephritic kidney, or sympathectomy, and possibly following toxemia of pregnancy.

The findings of the present study and the evidence cited favor a vasomotor, or neurogenic, origin of essential hypertension, a concept that had many proponents before Goldblatt's studies stimulated interest in the renal mechanism. It has been regarded by some[45] that hypertension is due to organic changes in the vasomotor center, i. e. medullary ischemia, but this view is not sustained by adequate factual data. Experimentally hypertension can be produced by procedures which decrease blood flow to the medulla.[46] It has been claimed that arteriosclerotic changes are found regularly in the small vessels of the medulla in hypertension and that excitation of the vasomotor center consequent to ischemia is responsible for hypertension.[47] Other studies,[48] however, have indicated that in the majority of cases of hypertension no evidence of arteriosclerosis

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of the vessels in the medulla in the region of the vasomotor center is found and that the region of the vasomotor center is morphologically intact. While hypertension in the majority of cases evidently cannot be ascribed to ischemia of the vasomotor center, it is of interest that "patients who had thickened arteries in this part of the brain without an accompanying elevation of blood pressure were not found." [48] It appears possible that arteriosclerotic changes in the region of the medulla may contribute to the genesis of hypertension in older age groups and that the exaggerated pressor response to vasomotor stimuli so frequently observed in elderly arteriosclerotic persons [49] may be on this basis.

Another mechanism influencing the vasomotor center has been considered in its possible relation to hypertension. Sustained elevation of the blood pressure can be produced experimentally by section of the moderator nerves from the carotid sinus and aorta.[50] However, there are no significant pathologic or physiologic changes in the carotid sinus in hypertension [51] and there is no evidence that carotid sinus reflexes acting on the vasomotor center play a causative role in hypertension.

The activity of the vasomotor center is influenced not only by such factors as blood flow to the medulla, oxygen and carbon dioxide tension, and carotid sinus reflexes, but also to a great degree by the cerebral cortex. Increasing attention is being paid to the psychosomatic factor in diseases peculiar to civilized man. Environmental influences, as well as heredity, play an undeniably important role in the genesis of essential hypertension. It has been abundantly demonstrated that hypertension is conspicuously rare in primitive races and in sedentary groups removed from urban civilization. Thus, hypertension is rare in African Negroes,[52] but its incidence is two and one-half times greater than in the white race among Negroes in metropolitan areas of the United States.[53] A distinct personality in hypertension was described some time ago by Moschcowitz [54] and more recently has been emphasized by numerous authors.[55] Essential hypertension is regarded as one type of manifestation of a psychoneurotic condition based on chronically excessive, inhibited, hostile (aggressive and competitive) impulses.[55] The sustained vasomotor stimulation resulting from such psychologic tension may ultimately lead to established hypertension. It is of interest that in schizophrenia, in which condition conflicts and frustration do not exist, owing to complete withdrawal from reality, the blood pressure is uniformly low.[56]

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SUMMARY

Blood pressure responses were studied in 35 cases of essential hypertension. Comparison was made in 30 cases between the pressor effects of breath holding and immersion of the hand in cold water, and the depressor response to sodium amytal, hyperventilation, pressure above the carotid sinus and combined hyperventilation and carotid sinus pressure. The maximum blood pressure levels attained with the breath holding and with the cold pressor tests were similar (breath holding 208/133, cold pressor 211/130). The depressor effect of hyperventilation or carotid pressure alone was not as great as that following sodium amytal, but when these two procedures were combined the lowest blood pressure level attained (157/94) corresponded quite closely to that resulting from sodium amytal (151/97). In 18 cases, including 13 of the aforementioned 30 cases, the pressor effect of inhalation of aromatic spirit of ammonia was compared with breath holding. The average maximal blood pressure attained with ammonia was 213/128, with breath holding 202/126. The ammonia test is particularly useful in subjects who cannot cooperate well in maintaining apnea sufficiently long to record blood pressure changes.

The variability of the blood pressure in hypertension makes single casual readings misleading. It is therefore preferable to record the blood pressure in terms of its maximum and minimum range. Employment of the breath holding or ammonia inhalation pressor test and the hyperventilation plus carotid pressure depressor test, as suggested, makes it possible to determine the range of the blood pressure with little more time or effort than is required to record the blood pressure routinely. In the 35 cases studied the blood pressure range determined with these procedures was 208/130-153/91.

Application of pressor and depressor tests as described makes it possible to differentiate between the humoral and neurogenic components in hypertension. Variations in carbon dioxide content of the blood induced by breath holding and hyperventilation, as well as carotid sinus pressure and various other pressor and depressor agents, alter the activity of the vasomotor center. The basal blood pressure level attained with depressor tests indicates the blood pressure relatively free of vasomotor influence. This basal level of blood pressure is maintained by humoral mechanisms, e. g. renal pressor (and possibly depressor) agents. The blood pressure influencing agents of the kidney (pressor and depressor) may exercise an important physiologic function in maintaining the basal "vital" level of the blood pressure. Superimposed on this a variable control is exercised by the vasomotor center in response to requirements determined by physiologic and environmental changes. The maximal effect of the neurogenic or vasomotor component is indicated by the blood pressure level attained with pressor tests.

There is no evidence to indicate that the renal pressor mechanism plays a part in the genesis of essential hypertension. The normal level of basal blood pressure observed in the earlier stages of hypertension suggests that in the initial stages of essential hypertension at least the humoral factor does not play an important role and that the neurogenic or vasomotor component is the more important determinant in the elevation of blood pressure. Thus, in 20 of the 35 cases studied, with an average maximal tension of 203/118 the basal blood pressure on depressor testing with inhibition of vasomotor control averaged 122/75.

With the development of organic lesions in the renal arterioles in the later stages of essential hypertension, and concomitant decreased renal blood flow, it is likely that the renal pressor mechanism ultimately comes to play a role in hypertension. That a humoral component does play a role in the later stages of hypertension and particularly in the malignant phase of essential hypertension is suggested by the failure of depressor agents acting on the vasomotor center, or sympathectomy, to decrease the blood pressure significantly. Hypertrophy of the muscular media which regularly occurs in hypertension may be a further factor in accentuating elevation of the blood pressure.

Heightened activity of the vasomotor center in essential hypertension cannot regularly be ascribed to organic changes such as arteriosclerosis of the medullary vessels with ischemia of the vasomotor system. In older age groups, however, this factor appears to be more significant. There is no evidence that abnormal activity of carotid sinus reflexes acting on the vasomotor center is of etiologic significance in hypertension. The activity of the vasomotor center is influenced greatly by the cerebral cortex, and psychosomatic factors appear to play an important role in the genesis of "essential" arterial hypertension.

CONCLUSIONS

The lability of the blood pressure in essential hypertension makes it desirable to record the maximum and minimum range rather than individual readings. This may be accomplished in simple fashion on routine examination by employing breath holding or brief inhalation of spirit of ammonia to attain the maximum pressor level, and by hyperventilation combined with carotid sinus pressure to obtain the basal depressor level. Application of these procedures makes it possible to differentiate humoral and neurogenic (vasomotor) components in hypertension. The basal blood pressure, which is largely determined by the humoral renal pressor mechanism, is normal in the earlier stages of hypertension, indicating that the humoral mechanism does not initiate the elevation of blood pressure in essential hypertension. In later stages, as the result of renal arteriolosclerosis and ischemia, the renal pressor mechanism becomes of greater importance. Hypertrophy of the arteriolar muscular media with an exaggerated response to stimuli may be a further factor in accentuating the elevated blood pressure. The heightened activity of the vasomotor center, which is responsible for the elevation of blood pressure in the earlier stages of essential hypertension, is probably to be attributed in large measure to psychosomatic influences. In older persons degenerative vascular changes in the medulla may be a contributing factor in heightened vasomotor pressor activity and hypertension.

THE TREATMENT OF INFLUENZAL MENINGITIS

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Meningitis due to Hemophilus influenzae is a not uncommon disease of infancy and early childhood. Both sulfonamides and specific rabbit antiserum have been used widely and with considerable success in the treatment of this infection for about five years. It seems appropriate at this time to sum up results obtained with the present treatment in order to facilitate the evaluation of new antibiotic substances when those effective against H. influenzae become generally available for clinical trial.

In 1922 Rivers,[1] in a review of the literature on influenzal meningitis, pointed out that the mortality rate in 200 reported cases was 92 per cent, or, in reality, even higher, since many cases are overlooked or not reported. He furthermore called attention to the fact that 12 of 17 patients who recovered were 2 years of age or older. Wilkes-Weiss and Huntington [2] in 1936 reviewed 500 cases and found a mortality of 97.6 per cent under the age of 2 and 79.5 per cent over the age of 2.

Immune goat serum,[3] bactericidal guinea pig serum [4] and Fothergill's immune horse serum were used in treatment between 1915 and 1939 with only slight effect on the mortality rates. Fothergill [5] in 1937 reported 201 cases treated with horse serum, the death rate being 84.6 per cent; these figures included Silverthorne's series of 36 patients with 11 recoveries and Schwentker's 17 cases with 5 recoveries.

At about the same time, reports began to appear in the literature of isolated cases treated with sulfonamides. Aléman [6] made an exhaustive survey of the literature up to 1940 and was able to collect from the literature and her own clinic in New Orleans reports of 82 cases treated with sulfanilamide, in which there were 10 recoveries. Six of the recovered patients were above 2 years of age.

Both Pittman [7] and Alexander [8] attempted to evaluate by means of mouse protection tests the relative efficacy of sulfanilamide, sulfapyridine and sulfadiazine in combating H. influenzae infection. Both found sulfapyridine superior to sulfanilamide and sulfadiazine most efficacious of all. It is not surprising, then, that recent journals contain reports of recoveries from influenzal meningitis following administration of sulfadiazine or some other sulfonamide alone. Sako, Stewart and Fleet [9] recently reported 23 cases; 13 patients received sulfadiazine only; 2 infants under 6 months of age died, while 11 patients recovered, 1 of them a 4 months

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old infant. Four of their patients received both sulfadiazine and horse serum: the 2 infants under the age of 2 months died, whereas the 2 older ones survived.

It seems clear then that the disease tends to be less severe in older children than in young infants, and that any suitable therapeutic agent brings about more recoveries among these older patients.

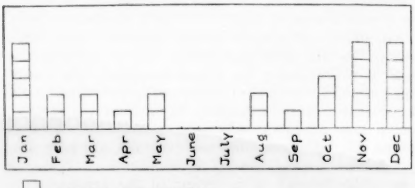

Chart 1.—Seasonal distribution of 28 patients with influenzal meningitis.

Working along lines suggested by Pittman's [10] earlier investigation, Alexander [11] in 1939 successfully prepared a potent rabbit serum against Hemophilus influenzae type B. She [12] herself reported the results of treating 50 patients treated with rabbit serum and sulfonamides, the mortality being 17 per cent in patients over the age of 7 months and 75 per cent in the younger age group.

The present series includes all of the proved cases of influenzal meningitis admitted to Sydenham Hospital since January 1941, at which time the Baltimore City Health Department and the Maryland State Department of Health made specific rabbit serum available to all patients regardless of their financial status.

SEASONAL INCIDENCE

The seasonal incidence of our cases (chart 1) corresponds to that originally pointed out by Rivers [1] in 1922, the greatest number occurring in November, December and January rather than in the late winter and early spring months, when other respiratory diseases are most prevalent.

AGE

The age distribution of these 28 patients is shown in chart 2 and corresponds to that pointed out by Fothergill and Wright [13] for influenzal meningitis in 1933 and by Waring and Smith [14] for pneumococcic meningitis in 1944. In this connection Fothergill and Wright studied the bactericidal power of whole defibrinated blood in various age groups and found that "with rare exceptions the blood of children between the ages of 2 months and 3 years has practically no bactericidal power against H. influenzae."

CLINICAL PICTURE AND BACTERIOLOGIC DATA

The clinical picture which the patients presented on admission varied considerably, as shown in the accompanying table. In all of these patients the diagnosis was established by finding H. influenzae in one or more spinal fluid cultures.

Some were alert but jittery; others appeared severely ill. None showed a rash, but in 20 of the 28 patients H. influenzae was grown from the blood. In 8 the organism was cultured from the nasopharynx, and about half of the patients had catarrhal otitis media. In 3 a hot, swollen joint was present on admission.

The variability of the clinical course is perhaps best indicated by the two following case reports:

Case 12.—A. G. was a 1 year old boy who, following an upper respiratory infection of four days' duration, developed convulsions and diarrhea, treated unsuccessfully at home with several doses of sulfadiazine. On admission he was restless, with a stiff neck and a temperature of 101.4 F. and seemed only moderately ill. The spinal fluid was cloudy; small gram-negative cocci were seen on smear and thought to be meningococci. The spinal fluid culture was sterile on culture. Sulfadiazine was given in the usual doses over an eight day period and the patient became asymptomatic. However, on the tenth day his temperature rose to between 102 and 103 F. At that time both blood and spinal fluid cultures became positive for H. influenzae type B. Sulfadiazine and rabbit serum were administered and the patient improved promptly. In retrospect it seems that the patient must have had mild influenzal meningitis on admission held in check by the sulfadiazine which he received both at home and after admission. The sulfadiazine being discontinued, he apparently relapsed until treated with serum as well as sulfonamide.

Case 17.—O. N., a boy aged 8 months, became ill quite suddenly on the night before admission with chills, fever, vomiting and later prostration. His temperature was 102.6 F. on arrival at the hospital and he seemed moderately ill. His spinal fluid was cloudy and loaded with H. influenzae organisms. Treated with sulfadiazine and specific rabbit serum as well as transfusion, he had fever spiking to 105 F. during the first week, later to 103 F. His course was very stormy for three weeks, and he had convulsions many times. Followed since discharge by his pediatrician, he has developed in every way normally.

Most noteworthy with regard to the spinal fluid findings are the reduction in spinal fluid sugar (as determined by the five tube method) and the frequency with which organisms were found on the admission smear and identified immediately by quelling with type specific serum. All but 1 of our cases was due to H. influenzae type B. The one exception, case 6, had a strain of H. influenzae in both blood and spinal fluid which could not be typed either in our own laboratory or by Dr. Hattie Alexander.

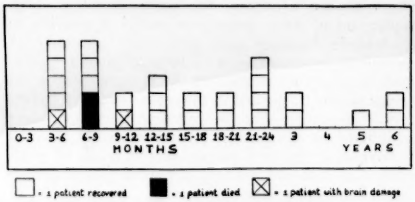

Chart 2.—Age incidence of influenzal meningitis.

THERAPY

Sulfonamides.—All of our patients received, in addition to specific rabbit antibody, one of the sulfonamide drugs in the manner and dosage previously outlined by us for the treatment of other types of meningitis.[15]

10. Pittman, M.: Variation and Type Specificity in Bacterial Species Hemophilus Influenzae, J. Exper. Med. **53**: 471, 1931.
11. Alexander, Hattie E.: Type B Anti-Influenzal Rabbit Serum for Therapeutic Purposes, Proc. Soc. Exper. Biol. & Med. **40**: 313, 1939.
12. Alexander, Hattie E.; Ellis, Catherine, and Leidy, Grace: Treatment of Type Specific H. Influenzae Infections in Infancy and Childhood, J. Pediat. **20**: 673, 1942.
13. Fothergill, L. D., and Wright, J.: Influenzal Meningitis: Relation of Age Incidence to Bactericidal Power of Blood Against Causative Organism, J. Immunol. **24**: 273, 1933.
14. Waring, A. J., Jr., and Smith, Margaret H. D.: Combined Penicillin and Sulfonamide Therapy in Treatment of Pneumococcic Meningitis, J. A. M. A. **126**: 418 (Oct. 14) 1944.
15. Hodes, H. L.; Smith, Margaret H. D., and Ickes, H. J.: Sixty Cases of Pneumococcic Meningitis Treated with Sulfonamides, J. A. M. A. **121**: 1334 (April 24) 1943.

We aimed to maintain a blood level of 8 to 12 mg. of sulfadiazine and 3 to 6 mg. of sulfapyrazine per hundred cubic centimeters, i. e. moderate rather than high drug levels. Sulfonamide therapy was continued for about two weeks after apparent clinical cure because of the well known tendency of patients with influenzal meningitis to relapse.

Fifteen of our patients received serum and sulfadiazine alone, with one death; 8 patients received serum and sulfapyrazine alone, and all recovered. The 5 remaining patients received more than one sulfonamide drug at some time during their illness. Obviously no final conclusion can be drawn from this small number of cases with regard to the relative merits of the two drugs. Nevertheless, it seems fair to say that the two are probably about equally effective. There is at least one other report in the pediatric literature of the use of sulfapyrazine in influenzal meningitis: Vandegrift [16] used sulfapyrazine twice in conjunction with immune rabbit serum, and 1 of his patients recovered. Sulfamerazine is also reported to be satisfactory.[17]

Clinical Data on Twenty-Eight Patients with Influenzal Meningitis

Case	Initials	Age	Month Admitted	Admission Cultures: Nasopharynx	Admission Cultures: Blood	Admission Spinal Fluid: Cell Count	Admission Spinal Fluid: Sugar	Admission Spinal Fluid: Smear	Clinical Picture: Temperature on Admission	Clinical Picture: Pneumonia	Clinical Picture: Otitis	Clinical Picture: Arthritis	Treatment: Drug *	Treatment: Rabbit Antibody, Mg.	Treatment: Serum Reaction	Result
1	B. J. S.	5 mos.	November	+	+	50	0	0	104.4	0	+	0	D+ Pz	325	0	Hydrocephalus
2	E. L.	6 mos.	January	+	+	160	0	+	102.4	0	0	0	D	75	..	Recovered
3	J. A. B.	6 mos.	January	0	+	2,000	0	+	103	0	0	0	Pz	275	+	Recovered
4	R. H.	6 mos.	November	0	+	500	Low	0	101	0	+	+	Pz	225	+	Recovered
5	J. M.	6 mos.	November	+	+	3,700	0	+	104.8	0	0	0	D+ Pz	300	+	Recovered
6	J. A.	7 mos.	December	0	+	1,700	0	+	104.8	+	+	0	D	...	..	Recovered
7	B. C.	8 mos.	August	0	+	2,500	Trace	+	103.4	0	+	0	D	300	0	Recovered
8	J. D.	8 mos.	February	0	+	1,840	Trace	+	101.4	0	0	0	Th+ D	275	0	Recovered
9	H. O.	9 mos.	January	0	+	5,400	0	+	104.4	0	0	0	D+ Pz	225	+	Died
10	F. F.	9 mos.	May	0	+	5,250	Low	0	104	+	+	0	D	225	0	Died
11	N. S.	10 mos.	March	+	?	8,000	0	+	101	+	+	0	D	250	0	Cortical atrophy
12	A. G.	12 mos.	April	0	+†	600	?	0	101.4	+	0	0	D	100	0	Recovered
13	W. F.	13 mos.	December	0	+	550	+	+	102	0	+	0	D	225	+	Recovered
14	G. T.	14 mos.	May	0	0	?	?	+	102.2	0	+	0	D	200	+	Recovered
15	K. P.	14 mos.	March	+	+	1,200	Trace	+	101.6	0	0	0	D	150	0	Recovered
16	D. S.	16 mos.	January	0	0	2,000	0	+	101	0	+	0	Pz	125+ 180 cc.‡	0	Recovered
17	O. N.	18 mos.	February	0	+	5,200	0	+	102.6	0	+	0	D	225	0	Recovered
18	L. L.	19 mos.	September	0	0	2,400	0	+	101	0	0	0	Pz	225	0	Recovered
19	D. M.	21 mos.	October	0	?	7,000	0	+	102	+	+	+	D	375	+	Recovered
20	J. Z.	22 mos.	October	0	+	3,500	0	+	103.8	0	+	+	Pz	250	+	Recovered
21	M. D.	2 yrs.	October	+	+	17,000	0	0	105.4	0	+	0	Pz	200	0	Recovered
22	S. H.	2 yrs.	August	0	0	700	Low	+	101.6	+	0	0	Pz	125	+	Recovered
23	G. H.	2 yrs.	November	+	+	2,80	Trace	+	103.4	?	0	0	Pz	250	+	Recovered
24	N. J. S.	3 yrs.	December	+	0	22,000	0	+	102	0	0	0	D	150	+	Recovered
25	D. M.	3 yrs.	November	0	0	12,500	0	+	103	0	+	0	D	225	+	Recovered
26	J. H.	5 yrs.	December	0	+	5,0.0	0	+	102.6	0	0	0	D+ Pz	150	0	Recovered
27	F. H.	6 yrs.	January	0	+	120	Normal	+	102	0	0	0	D	40+ 40 cc.‡	0	Recovered
28	F. A.	6 yrs.	December	0	+	20,0.0	?	+	101.8	0	0	0	D	150	0	Recovered

* D, sulfadiazine; Pz, sulfapyrazine; Th, sulfathiazole. † At the time of relapse. See case report.
‡ In 2 cases unstandardized serum of low titer was used.

Serum.—Twenty-seven of our 28 patients were treated with anti-H. influenzae type B rabbit serum, the 1 exception being the patient with an untypable strain of organism. In our earlier experience the initial dose of serum was 50 to 75 mg. of antibody nitrogen, but we have gradually come to feel that the initial dose should be relatively large. At present, in a severe case, 125 to 150 mg. is given soon after admission.

The subsequent dosage of rabbit antibody is determined as outlined by Alexander, assaying each day varying dilutions of the patient's own serum against a subculture of the organisms originally recovered from his own spinal fluid. Sufficient serum is administered so that the patient's own serum in a dilution of approximately 1:16 will produce capsular swelling of the stock culture. As the patient improves, the organisms die off and cease to produce specific soluble polysaccharide, which combines with the specific antibody. Thus the rate of disappearance of the rabbit antibody slows down and approximates the rate of destruction of any heterologous serum. Conversely it is a good prognostic sign if the patient almost maintains his antibody titer from day to day without further administration of serum.

The total dose of serum has varied in our cases from 75 mg. (the first case treated) to 325 mg., the average being 200 to 250 mg.

Twenty-five of the 27 patients treated with serum received all or most of this serum intravenously. Two patients (24 and 27) received intramuscular serum only with excellent results. This mode of administration, first reported by Boisvert and his associates,[18] should probably be used much more often, as it obviates some of the severe serum reactions observed after intravenous therapy. One patient (1) whose spinal fluid cultures remained positive received intrathecal serum as a last resort, without apparent beneficial effect.

It has been our practice to follow a suggestion originally made by Neter:[19] the patient is given a small desensitizing dose of rabbit serum at least every five days until all need for serum therapy is definitely past.

Lumbar Punctures.—In order to plan properly for the dosage of serum and the duration of sulfonamide therapy, it is essential to follow closely the changes in the spinal fluid. Although a patient with meningococcic meningitis is rarely subjected to more than one lumbar puncture, we feel that patients with influenzal meningitis should be tapped daily until the spinal fluid cultures have been sterile for several days and until the spinal fluid sugar has returned to normal.

16. Vandegrift, H. N.: Experience with Sulfapyrazine in Children, J. Pediat. **25**: 386, 1944.

17. Hall, W. H., and Spink, W. W.: Sulfamerazine: Clinical Evaluation in 116 Cases, J. A. M. A. **123**: 125 (Sept. 18) 1943.

18. Boisvert, Paul L.; Fousek, Mildred D., and Grossman, Marya F.: Intramuscular Administration of Anti-Hemophilus Influenzae, Type B, Rabbit Serum: Report of Its Use in Three Cases of Influenzal Meningitis, J. A. M. A. **124**: 220 (Jan. 22) 1944.

19. Neter, E.: Observations on Hemophilus Influenzae (Type B) Meningitis of Children, J. Pediat. **20**: 699, 1942.

Mastoidectomy.—Many of our patients showed mild otitis media on admission. In a few instances myringotomy was necessary, but in none of our cases did mastoidectomy appear to be indicated. We feel that the indications of mastoidectomy should be the same whether meningitis is present or not, and that a patient who is suffering from a severe disease such as meningitis should not be subjected to a major operation unless such a measure seems unavoidable.

General Measures.—Intravenous fluids were employed as indicated, and transfusions were given whenever the patient's hemoglobin on admission was below 10 Gm.

COMPLICATIONS OF SERUM THERAPY

The use of the anti-H. influenzae rabbit serum has unfortunately certain unpleasant side effects of minor importance. Perhaps because this serum is less completely purified than certain others in common use, serum reactions are relatively frequent. Our records show that 12 of our 27 patients treated with serum had side reactions. These reactions seem to fall into three types:

(*a*) Immediate anaphylactoid reactions, of which we saw 2 examples. In one 6 months old infant intravenous administration of 125 mg. of rabbit antibody was followed immediately by a severe reaction consisting of fever, cyanosis and asthmatic breathing. The symptoms abated rapidly after administration of epinephrine. The other patient was a 9 months old infant who, to judge by the history, must have had meningitis for a month before admission. After receiving a few cubic centimeters of rabbit serum intravenously he became stiff, cyanotic and apneic. He was finally revived with intracardiac epinephrine. Immediate and severe reactions to serum when administered to very ill patients have been seen by us and described by others [20] as occurring in conjunction with the administration of serum to patients with pneumonia. Their cause is unknown.

(*b*) An interesting type of delayed reaction occurred in 4 of our patients. Routine tests for sensitivity to rabbit serum are given our patients by dropping into one eye a small amount of the material diluted 1:10. Several showed on the following day edema and slight reddening of the soft tissues about the eye which persisted for another two to three days. The conjunctiva was slightly inflamed at the same time.

(*c*) The commonest type of serum reaction was serum sickness, which appeared between the ninth and twenty-third hospital days and was characterized clinically by an urticarial rash in all cases and in most by fever and painful joints in addition. One patient showed fever at the end of the second week in the hospital which could not be accounted for on the basis of the clinical findings and which may have represented abortive serum sickness.

We wish to stress the frequency with which we encountered serum reactions, not because they militate against the use of the serum but because they enforce care in its administration and frequently provide the explanation for fever, malaise and rash occurring late in the course of the disease when the patient was thought to have recovered. Also these reactions in many cases prolong convalescence.

20. Wood, W. B.: Studies on Mechanism of Recovery in Pneumococcal Pneumonia, J. Exper. Med. **73**: 201, 1941.

RESULTS

Twenty-four of the 28 patients apparently recovered completely, without sequelae. Seven of these were aged 8 months or less. The following 5 were thought at the time of discharge to show evidence of brain damage:

Patient 2 went home with questionable hydrocephalus but on subsequent follow-up was found to be entirely well.

Patient 8 had some spasticity of one arm.

Patient 11 appeared a complete idiot both on discharge and when seen a year later.

Patient 1 was suffering from severe hydrocephalus.

Patient 18 had mild spastic hemiplegia.

Two of the 28 patients died, a mortality of 7 per cent. One of these, a 9 months old infant, has already been mentioned as having had an anaphylactic reaction on administration of serum. His illness had been of long duration before he came to us and his outlook appeared hopeless from the first. The other patient who died was likewise 9 months of age. There was a delay of two days in her case in starting specific therapy, since the diagnosis was made only on the basis of a positive spinal fluid culture. Moreover, the serum was not given at the beginning in our usual high dosage but rather in smaller divided doses over a period of ten days. At any rate, whatever the reasons, the patient succumbed on the twenty-ninth hospital day.

Instead of speaking of the percentage of deaths following influenzal meningitis, it is probably actually more accurate to group on the one hand those patients who were discharged in satisfactory condition and, on the other, those who died or who were severely crippled. On this basis, we can say that 24 (85 per cent) of our patients did well and that 4 (15 per cent) did not respond satisfactorily: either they died or showed evidence of severe and presumably permanent damage to the central nervous system.

COMMENT

From the bacteriologic point of view patient 6 is of some interest in that the organism recovered from his spinal fluid did not fall into any of the established types of H. influenzae; nor was it found to give with the standard types of antipneumococcus rabbit serum any of the cross reactions which have been described from time to time in connection with strains of H. influenzae.[21] Although most cases of H. influenzae meningitis are due to type B, other types have occasionally been recovered from the spinal fluid.[22] In general, meningitis due to type B is more severe than that due to other types.[23]

The relatively high recovery rate among our very young patients is, we think, dependent on at least two factors. In the first place all of the patients admitted to this hospital are carried immediately into an admission room, where the necessary diagnostic and therapeutic procedures are carried out as expeditiously as possible. Unnecessary manipulation and loss of time in instituting treatment have a deleterious effect on any

21. Zepp, H. D., and Hodes, H. L.: Antigenic Relation of Type B H. Influenzae to Type 29 and Type 6 Pneumococcus, Proc. Soc. Exper. Biol. & Med. **52**: 315, 1943. Chapman, O. D., and Osborne, W.: Serological Relationships Between Diplococcus Pneumoniae and Hemophilus Influenzae, J. Bact. **44**: 620, 1942. Neter, E.: Antigenic Relationship Between H. Influenzae Type B and Pneumococcus Type VI, Proc. Soc. Exper. Biol. & Med. **52**: 289, 1943.

22. Gordon, J.; Woodcock, H. E. de C., and Zinnemann, K.: Meningitis Due to Pittman and Non-Pittman Strains of H. Influenzae, Brit. M. J. **1**: 779, 1944. Birdsong, M.; Waddell, W. W., Jr., and Whitehead, B. W.: Influenzal Meningitis, Am. J. Dis. Child. **67**: 194 (March) 1944.

23. Alexander, Hattie E.: Personal communication to the authors.

severely ill person. In the second place the patients seem to do better when given larger doses of serum early in the illness. In this way the patient is certain to have in his blood at all times an excess of antibody. Moreover, it is theoretically possible in this way to increase the amount of antibody supplied to the spinal fluid without the risk of producing block due to the serum itself, a risk which is not negligible when animal serum as such is introduced into the subarachnoid space. That the antibody titer of the spinal fluid is proportional to that of the blood in a ratio of approximately 1:300 has been shown by Freund [24] following both active and passive immunization of rabbits against typhoid. Ramon and Descombey [25] demonstrated a similar relationship with regard to antitoxin in serum and spinal fluid, and Morgan and her associates [26] described the same ratio following active immunization with the viruses of both eastern and western equine encephalomyelitis. That antibody is present in the spinal fluid following intravenous administration of anti-influenzal rabbit serum has been shown by Alexander,[8] although the exact ratio has not to our knowledge been determined.

Our experience sheds no light on the much discussed question of using intrathecal serum in the treatment of patients who do not respond to the use of intravenous or intramuscular serum combined with sulfonamides. Most of our patients are seen and treated early in the course of the disease, and, owing either to chance or to the use of large doses of serum, seem to recover without intrathecal serum.

In summary, then, we find on the basis of 28 consecutive cases that the intensive use of sulfonamide and specific serum therapy in influenzal meningitis has reduced the mortality until it is comparable to that of meningococcic meningitis. The high cost of the serum, the tedious and repeated determinations of the patient's serum titer and the high incidence of serum reactions lead us to hope that new antibiotic substances will soon "streamline" the treatment.

SUMMARY

1. Twenty-eight consecutive cases of influenzal meningitis have been treated at this hospital since 1941.

2. The seasonal incidence seems to be highest in late autumn and early winter.

3. The age incidence of influenzal meningitis in infancy follows a curve roughly similar to that of pneumococcic meningitis, i. e. the maximum number of cases occur between the ages of 3 and 9 months.

4. Early diagnosis and intensive early therapy, using both sulfonamides and type specific rabbit antibody, have reduced the mortality to a figure comparable to that of meningococcic meningitis. Failure to use serum early in the course of treatment entails unnecessary risk to the patient's life.

5. The mortality has been most strikingly lowered in the younger infants, among whom the mortality is highest.

6. Sulfapyrazine and its sodium salt have been found to be effective in the treatment of this disease.

7. The incidence of serum reactions is high but does not militate against the use of serum.

Harford Road and Herring Run, Baltimore 12.

24. Freund, J.: Accumulation of Antibodies in Central Nervous System, J. Exper. Med. **51**: 889, 1930.
25. Ramon, G., and Descombey, P.: Sur le passage des antitoxines à travers la barrière méningée, Compt. rend. Soc. de biol. **108**: 358, 1931.
26. Morgan, Isabel; Schlesinger, R. W., and Olitsky, P. K.: Induced Resistance of Central Nervous System to Experimental Infection with Equine Encephalomyelitis Virus, J. Exper. Med. **76**: 357, 1942.

CENTRAL NERVOUS SYSTEM COMPLICATIONS ASSOCIATED WITH KERNICTERUS

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Kernicterus as a pathologic finding has been observed almost exclusively in children that have exhibited the clinical picture of erythroblastosis fetalis. It is therefore a reasonable conclusion that this type of cerebral abnormality in the vast majority of cases is the result of maternal isoimmunization during pregnancy primarily by the Rh factor.

While the neonatal mortality rate in children with kernicterus is very high, a certain number do survive for a variable period. The recognition of these cases in the past has depended on the history of severe neonatal jaundice and the subsequent development of symptoms of central nervous system disease. Most of the reported cases of this type presented a clinical picture in which evidence of basal ganglion injury predominated, such as choreoathetosis and extrapyramidal spasticity.[1] The widespread nature of neuronal damage in kernicterus [2] suggests the possibility that certain of the surviving patients might present other types of neurologic defects. Kernicterus has been demonstrated in infants, moreover, in whom neonatal jaundice or other signs of erythroblastosis fetalis were relatively inconspicuous.[3] Since neither the clinical picture nor the neonatal history need be absolutely characteristic, it seems clear that a further evaluation of the syndrome is indicated.

Mental deficiency is the most common manifestation of extensive cerebral abnormality of prenatal origin. It would appear likely that among large groups of congenitally severely retarded children one might expect to find a small number in whom the cerebral defect was the result of maternal Rh isoimmunization.

That this might be the case was suggested by a preliminary study [4] in which it was found that the incidence of mother-child Rh incompatibility was significantly greater among a group of undifferentiated defectives as compared to a control group consisting primarily of mongolians, spastic diplegias and postinfectious and post-traumatic types.

Our purpose in this paper is to present the results of a much wider study of this kind and to describe briefly some of the clinical conditions encountered that might represent this type of cerebral damage.

MATERIAL AND METHODS

There were in the institution at the time of this study approximately 350 children with intelligence quotients of less than 30. Of the mothers of these children it was possible to obtain at least one blood sample on 277. Of the remainder, a small number were deceased, many failed to respond to one or more written requests to visit

Published under the auspices of the Section on Nervous and Mental Diseases.
Supported by a grant from the Fluid Research Fund, Yale University School of Medicine.
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1. Zimmerman, H. M., and Yannet, Herman: Cerebral Sequelae of Icterus Gravis Neonatorum and Their Relation to Kernicterus, Am. J. Dis. Child. **49**: 418 (Feb.) 1935.
2. Zimmerman, H. M., and Yannet, Herman: Kernicterus, Am. J. Dis. Child. **45**: 740 (April) 1933.
3. Unpublished personal observations. Zimmerman and Yannet.[3]
4. Yannet, Herman, and Lieberman, Rose: The Rh Factor in the Etiology of Mental Deficiency, Am. J. Ment. Deficiency **49**: 133, 1944.

the laboratory, and some could not be located. Studies of the children's blood were carried out only on those whose mothers proved to be Rh negative.

Of the 277 children it was possible to place 158 into well recognized diagnostic classifications, including 45 mongolians, 33 with infantile spastic diplegia and 36 with acquired defects due to cerebral infections or trauma. Also included were cases of phenylpyruvic amentia, craniofacial anomalies, tuberous sclerosis, cerebral lipoidoses and other conditions. These were treated as the control group. The remaining 119 children diagnosed as undifferentiated made up the group in whom the incidence of mother-child Rh incompatibility was being investigated. Before being diagnosed as undifferentiated, every clinical and laboratory facility was employed to rule out known etiologic categories. However, it is appreciated that included in the group are an undetermined number of cases based on recessive genetic factors which could not be diagnosed because of small sibships or lack of adequate family histories. Also included are probably cases of birth trauma without characteristic history or examination, as well as fetal injuries due to maternal illnesses of which no record was available. Prenatal, neonatal or infantile encephalitic processes may also have been inadvertently included. It is therefore clear that if the Rh factor was of etiologic importance in explaining some of the cases in the undifferentiated group, the expected proportion would be relatively small, although significantly greater than one would expect to find in a control group.

Results of Blood Examination

	Total Number	Mother Rh —	Mother Rh — Child Rh +
Control	158	22 (14.0%)	12 (7.6%)
Undifferentiated	119	26 (22.0%)	19 (16.0%)

The anti-Rh serum used was obtained through the courtesy of Dr. Diamond from the Blood Grouping Laboratory in Boston. The method used for typing was that described by Levine.[5] Maternal Rh antibodies were also determined whenever possible, including the so-called "blocking" antibodies, as described by Wiener.[6]

RESULTS

The results are summarized in the table. Approximately 14 per cent of the mothers in the control group were Rh negative. This agrees with the ratio to be expected on the basis of random selection. The random distribution of the Rh factor is such that an Rh negative woman has a 60 per cent chance of giving birth to an Rh positive child.[7] On this basis the 22 Rh negative mothers in the control group might be expected to have 13 Rh positive children, giving 8.2 per cent as the theoretical or random ratio of mother-child Rh incompatibility. This agrees with the actual finding, as the table indicates, of 12 cases (7.6 per cent) of Rh incompatibility in the control group. In the undifferentiated group, on the other hand, 26, or 22 per cent of the mothers, were found to be Rh negative. Moreover, whereas one might have expected to find 15 or 16 Rh positive children in this group, actually 19 were found, giving a ratio for mother-child Rh incompatibility of 16 per cent in the undifferentiated group as compared to 7.6 per cent in the control group. The difference between these ratios is statistically significant.

On the basis of the findings in the control group as well as on theoretical considerations, only 9 cases of mother-child Rh incompatibility should have been found in the 119 cases in the undifferentiated group; actually 19 were encountered. It would therefore seem reasonable to expect that of the 19 cases approximately 10 may represent examples of cerebral damage due to maternal Rh isoimmunization.

The identification of those cases which definitely represent examples of fetal injury due to maternal Rh isoimmunization presents a problem which cannot be entirely solved as yet. A clinical appraisal of the 19 cases in which isoimmunization was possible on the basis of blood incompatibilty yields three fairly distinct groups. These are now summarized:

Group 1.—This group includes 3 cases in which there is definite evidence of maternal isoimmunization. In cases 1 and 2 high titers of Rh antibodies were found in the mothers five and three years after delivery respectively, while in case 3 the mother died in 1942 following a transfusion of Rh positive blood administered soon after the delivery of a child who died with typical erythroblastosis fetalis. A brief clinical description of these cases follows:

Case 1.—W. V., a boy, was born Dec. 9, 1939, the result of the second pregnancy, which was entirely uneventful. The preceding pregnancy in 1938 terminated at 7 months with the delivery of a dead fetus. A report from the hospital gave the cause of death as "intrauterine asphyxia" with little qualifying details. The mother at this time was given a transfusion because of postpartum bleeding, the husband, who was Rh positive, acting as donor. No reaction to this transfusion was recorded. The patient was delivered without difficulty after a four hour labor. On the third day he developed jaundice and fever, and blood studies were reported by the hospital as being characteristic of erythroblastosis fetalis. Peculiar spasms, first noted at the end of the first month, became gradually more frequent, so that by the third month there was generalized spasmodic increase in muscle tone. Abnormal, athetoid-like movements of the extremities appeared one month later and persisted. Periods of opisthotonos also became evident. There was no sign of any significant mental development. He was admitted to the Southbury Training School on Dec. 28, 1944 at 5 years of age. Examination revealed a decidedly emaciated child whose mental age was estimated at 5 months. The head measured 47.5 cm. in circumference and there was a moderate degree of athetosis of the extremities, most pronounced in the left arm, and some facial grimacing. Although muscle tone was usually increased, there were short periods of relaxation during which hypermobility was quite striking at the hips, knees, ankles and wrists. Deep tendon reflexes could be obtained only with difficulty. There was no ankle clonus, but the Babinski responses were bilaterally extensor. Tonic neck reflexes could frequently be elicited. Laboratory findings were consistently within normal limits. The remainder of the examination was not contributory. The child was admitted to our hospital on four occasions in the following five months with upper respiratory infections, during which no peculiarity was noted in the temperature course. There has been no significant change in the clinical picture since admission.

Case 2.—M. J. Mc., a boy, was born Sept. 19, 1941, the product of the second pregnancy. An older sibling born in 1940 is Rh positive, had a normal neonatal period and was found to be entirely normal in 1944. There was a third pregnancy in 1943, resulting in an Rh positive infant who survived a stormy neonatal period during which a characteristic picture of erythroblastosis fetalis was present, requiring frequent transfusions. The latter child was found to be entirely normal at 14 months of age. The patient was born after an uneventful pregnancy

5. Levine, Philip: The Pathogenesis of Erythroblastosis Fetalis, J. Pediat. **23**: 656 (Dec.) 1943.
6. Wiener, A. S.: A New Test (Blocking Test) for Rh Sensitization, Proc. Soc. Exper. Biol. & Med. **58**: 173 (June) 1944.
7. Morgan, W. T. J.: Occurrence and Nature of Human Blood Group Substances, Brit. M. Bull. **2**: 165, 1944.

and uncomplicated, short labor. Jaundice appeared on the second day and became intense during the following days. Head retraction and generalized short muscle spasms appeared on the third day and persisted to a more or less noticeable degree, especially when disturbed. No transfusions were required and the child was discharged on the tenth day, with the jaundice practically gone. Abnormal movements of the extremities were first noted at the fourth month. No significant mental development was evident. Feeding was always difficult and associated with much coughing and gagging.

The child was seen frequently by physicians because of hyperpyrexia, occasionally associated with signs of respiratory infection but frequently without evident cause. He was admitted to the Southbury Training School on Oct. 19, 1944 at the age of 3 years. Examination at this time indicated that the boy was extremely malnourished with a mental age estimated at 3 months. The head was symmetrical and measured 50 cm. in circumference. The only significant findings were in the central nervous system. There was athetosis of the extremities, more pronounced on the left side. The head was held rotated to the right, and there was constant facial grimacing. The muscle tone was increased irregularly in all extremities most of the time. This child, as in case 1, also exhibited, during periods of relaxation, accentuated hypermobility at the knee, ankle and wrist joints. The deep tendon reflexes could not be obtained, and the Babinski responses were equivocal. Studies of the blood, urine and spinal fluid were within normal limits. The course was characterized by episodes of unexplained fever frequently over 104 F. Blood cultures on three occasions during these periods were sterile. On Feb. 2, 1945, about four months after admission, the child died exhibiting hyperpyrexia without significant clinical signs of infection. At autopsy a small quantity of thick pus was found in the right mastoid cells, although otoscopy shortly before death showed no significant abnormalities in the canals or tympanic membranes. The lungs showed a focal lipoid pneumonia. The brain and spinal cord was examined by Dr. S. H. Durlacher of the pathology department of the Yale University School of Medicine. The findings were essentially similar to those previously reported by Zimmerman and Yannet [1] both in distribution and in the nature of the changes, so that a detailed description is not included. Briefly, widespread but patchy demyelinization and loss of ganglion cells characterized the findings. This was especially prominent in the basal ganglions.

CASE 3.—T. W., a boy, was the result of the third of five pregnancies. The first two children, born in 1934 and 1935 respectively, had normal neonatal histories and showed subsequent normal and uneventful development. The fourth pregnancy, in 1940, terminated in the delivery of a stillborn child. The fifth pregnancy, in 1942, also resulted in a stillborn child. During this postpartum period, because of a hemorrhage, the mother was transfused, a professional donor being employed. A severe reaction ensued, resulting in the death of the mother. Subsequent study showed that the mother's blood was Rh negative and the donor's Rh positive.

The patient was delivered without difficulty on Oct. 2, 1938 and appeared normal at birth. Within twelve hours he developed a rapidly increasing jaundice and severe anemia. A diagnosis of erythroblastosis fetalis was made, and the child was transfused repeatedly. He made a gradual recovery and seemed in good condition when discharged three weeks later. It soon became apparent that his development was significantly retarded. He failed to sit alone before the second year and began to walk during the third year. He made no effort to talk. There was no history of abnormal motor activity or convulsions. He was admitted to the Southbury Training School on March 16, 1943 at 4½ years of age. At this time he was well nourished and had a mental age of 2 years. He made no effort to talk but could understand and carry out simple commands. The head was symmetrical and measured 50 cm in circumference. The significant findings were confined to the examination of the central nervous system. The gait was grossly ataxic, with internal rotation of the feet. There was a well established lumbar lordosis. Definite genu recurvatum was present bilaterally, more pronounced on the right. There was an alternating strabismus with normal fundi. A generalized hypotonia could be demonstrated, which was symmetrical in distribution. There was well defined ataxia of both upper extremities and the trunk. No abnormality in exteroceptive sensation was present. The deep tendon reflexes were easily obtained and equal. The Babinski responses were flexor, and the abdominal reflexes were present. The course in the institution was characterized by a slow but definite improvement in motor activity. The gait improved considerably, so that locomotion became relatively adequate, although ataxic. His speech has shown favorable progress, although still greatly retarded. The hypotonia and associated muscle weakness is still evident but less definite. His mental age is estimated, at this time (June 1945) at 3 years, giving the boy an intelligence quotient of about 45.

GROUP 2.—The next 3 cases are grouped together because, although the evidence for maternal Rh isoimmunization was presumptive, it was not as definite as in the preceding group. In cases 4 and 5 no Rh antibodies could be demonstrated in the mothers, while in case 6 serum could not be obtained for study. Also patients 4 and 5 were born at home, and because they were relatively older (19 and 20 years respectively) the neonatal histories, as obtained from the mothers, were not considered accurate or adequately detailed. However, as the following brief summaries will indicate, it was likely that all of these children had erythroblastosis fetalis.

CASE 4.—N. J., a boy, was one of twins, born without difficulty at the end of the fifth pregnancy, which was uneventful. The other twin, a girl, was said to have been entirely normal in development. Unfortunately she could not be reached for blood examination. The preceding 4 children, born in 1914, 1917, 1923 and 1925 respectively, were said to be normal but were also unavailable for study. A sixth pregnancy, in 1934, ended in a miscarriage at 5 months, and the seventh pregnancy resulted in a full term stillborn fetus.

The patient was born Dec. 19, 1926 at home, attended by a midwife. He seemed normal at birth. On the third day he was noticed to be jaundiced and very pale. The following day he had a generalized convulsion, followed by numerous cyanotic spells. He did poorly during the following two months, gaining little weight. At about 4 months of age, abnormal movements of the extremities became apparent and persisted. His development was greatly delayed. He could not support his head until 2 years of age; he sat alone at 3 years and walked at 9 years. Speech was never intelligible. He was admitted to the Southbury Training School on Nov. 2, 1944 at 18 years of age. Examination at this time revealed that he was moderately well nourished and that his mental age was estimated at about 3 years. His head was symmetrical and measured 50 cm. in circumference. There was generalized athetosis, with facial grimacing. The head was held rotated to the right. The gait was suggestively ataxic, and there was evidence of incoordination in the use of his arms. There was sustained increase in muscle tone with no definite periods of relaxation, as was exhibited in cases 1 and 2. The deep reflexes were equal and of normal intensity. The Babinski responses were flexor; the abdominal reflexes were obtained with difficulty, and ankle clonus was absent. The remainder of the examination was not significant. Laboratory findings were not abnormal. The boy's course has been relatively uneventful since admission, and his condition at present is unchanged.

CASE 5.—T. S., a girl aged 19 years, was the result of the first pregnancy, which was uneventful. A second pregnancy, in 1938, resulted in a normal child who was found to be Rh negative. The patient was born at home, attended by a physician after an uncomplicated delivery. During the first week there were many attacks of cyanosis. Jaundice appeared early and became intense during the first week, lasting for almost four weeks. The stools were of normal color. Around the fourth month, abnormal movements appeared and persisted. At 7 months of age she had generalized convulsions, which were repeated infrequently during the next year but have not recurred since. Development was greatly retarded. She began to walk alone at 7 years. Speech is still almost unintelligible. She

was admitted to the Southbury Training School on Jan. 27, 1944. Examination at this time showed that she was well nourished, and her mental age was estimated at about 5 years. The head was symmetrical, measured 54 cm. in circumference and was held turned to the right. Generalized athetosis was prominent and the gait suggestively ataxic. There was spasmodic increase in muscle tone, but, during periods of relaxation, definite hypotonia was present with hypermobility at the wrists, knees and ankles. Deep reflexes were difficult to elicit, the Babinski responses were equivocal, abdominal reflexes were present and ankle clonus was absent. The remainder of the examination was not remarkable. Laboratory studies were noncontributory. The girl made a good adjustment to her institutional experience, and her present status is essentially unchanged.

CASE 6.—C. S., a girl aged 7 years, was the result of a full term, uneventful second pregnancy. The first child was stillborn after a long labor said to have lasted for five days. The cause of death was given as "birth trauma." The patient was delivered without difficulty in a hospital and seemed normal at birth. On the third day jaundice was noted. This became intense rapidly and was said to have persisted for over four weeks. On the third day she developed spasmodic episodes with head retraction. These occurred frequently but gradually subsided by the end of the third week. Around the fourth month increased muscle tone became evident, increasing in severity and persisting. The girl never walked or talked and has been confined to bed. At 6 years of age she began to have generalized convulsions, which recurred at infrequent intervals. She was admitted to the Southbury Training School on June 6, 1943. At this time she was poorly nourished, and her mental age was less than 6 months. The head was symmetrical and measured 49 cm. in circumference. There was no evidence of abnormal movements. There was a generalized but irregular increase in muscle tone that was constant and could be overcome only with considerable force. Fingers were held hyperextended at the metacarpophalangeal joints and flexed at the terminal phalangeal joints. The deep reflexes were hyperactive but equal; there were bilateral ankle clonus and bilateral extensor Babinski responses. The abdominal reflex was absent on the right but present on the left. The fundi were negative. There was gross incoordination of the extraocular movements, and light perception was present. Except for the emaciation and underdevelopment, the remainder of the examination and the laboratory studies were not remarkable. The child remained at the institution for about three weeks and was taken home against advice. There had been no significant change.

GROUP 3.—The remaining 13 cases are grouped together because of the absence of any significant findings in the histories that would in any way suggest the possibility of isoimmunization in the mothers. Unfortunately, the relatively advanced ages of the patients (average age 24 years) and the fact that the majority were born at home made the neonatal histories, as obtained from the mothers, difficult to evaluate. In about half the cases it was possible to obtain specimens of serum from the mothers for study, but no evidence of Rh antibodies could be demonstrated. Unfortunately the more sensitive slide agglutination method for demonstrating Rh antibodies recently described by Diamond and Abelson [8] was not available. However, on the basis of the incidence of mother-child Rh incompatibility found in our control group it is not unlikely that a few of these do represent instances of cerebral damage on the basis of Rh isoimmunization. However, the clinical picture was in no way characteristic. Eleven were males, and five were first born. There were 4 children who were premature. In 2 of these there was a family history of prior stillbirths. In 1 case a preceding pregnancy had terminated in the delivery of an infant that died at 4 days of age with jaundice, but the data were too meager to warrant a diagnosis. The physical findings were characterized by the absence of signs of specific central nervous system abnormalities except for the severe mental defect. In brief, although there is reasonably good evidence that some of these cases do fall into the group of brain injuries due to Rh isoimmunization, a positive or even a presumptive diagnosis in any individual case was impossible at this late date. The consideration of this possibility seems indicated in every case of mother-child Rh incompatibility, so that evidence of isoimmunization in the mother and the less dramatic signs of erythroblastosis fetalis in the child can be sought for relatively soon after birth. Only in this way will it be possible to be sure that some of the cases that are included in group 3 actually represent atypical examples of kernicterus.

COMMENT

Most of the cases in groups 1 and 2 in which a definite or presumptive diagnosis of maternal Rh isoimmunization could be made show essentially the same clinical picture previously described of surviving patients with kernicterus.[9] This included a stormy neonatal period (now recognized clinically as erythroblastosis fetalis), the early appearance of increased muscle tone followed soon after by abnormal movements of the extremities and relatively severe mental defect. The clinical picture in case 3, however, was strikingly different. The neurologic defect was almost entirely confined to cerebellar dysfunction, while the mental defect, although obvious, was distinctly less than in the other cases. Suggestive evidences of possible cerebellar dysfunction also could be demonstrated in cases 1, 2, 4 and 5, although the signs were overshadowed by the other manifestations of central nervous system injury, of which those referable to the basal ganglions predominated. The presence of signs of cerebellar involvement is not surprising in view of the well defined changes that have been demonstrated in the dentate nucleus in a previously reported postmortem study of this condition.[1]

While the evidence is highly suggestive that a certain number of the cases in group 3 represent bona fide examples of cerebral injury due to maternal Rh isoimmunization, it is nevertheless based almost entirely on statistical considerations. It is apparent that further confirmatory evidence is necessary in this respect. A recent report by Snyder, Schonfeld and Offerman [10] is of interest. These investigators carried out a somewhat similar study of the mothers of 68 institutionalized undifferentiated mental defectives and found almost twice the number of Rh negative mothers and incompatible mother-child relationships than should have been present on the basis of random selection. However, as was stated earlier, definite proof of isoimmunization in the mother and of manifestations of erythroblastosis fetalis in the child should be sought for in every case of Rh incompatibility no matter how benign the neonatal period, and this correlated with the subsequent development of the child. It will be primarily through this type of follow-up that validity will be given to what must remain at present a reasonable possibility at best.

It should be noted that our present studies, for reasons previously stated, have been confined to children in the low imbecile and idiot categories. That lesser

8. Diamond, L. K., and Abelson, Neva M.: The Demonstration of Anti-Rh Agglutinins: An Accurate and Rapid Slide Test, J. Lab. & Clin. Med. **30**: 204 (March) 1945.

9. Zimmerman and Yannet, footnotes 1 and 2.

10. Snyder, L. H.; Schonfeld, M. D., and Offerman, E. M.: The Rh Factor and Feeblemindedness, J. Hered. **36**: 9 (Jan.) 1945.

degrees of cerebral injury associated with only slight evidence of mental defect and neurologic abnormalities may also result from this sensitization mechanism remains to be evaluated. It is evident that the obstetrician and pediatrician must be alert to the possibilities of this type of fetal injury so that pertinent observations may be made at the most opportune time.

The pathogenesis of the central nervous system injury resulting from maternal isoimmunization is at present unknown. On the basis of our present knowledge, the following tentative hypotheses may be postulated. It has been demonstrated by Boorman and Dodd [11] that in Rh positive individuals the Rh factor is present in practically all tissues, although in small amounts, when compared to the agglutinogens A and B. The possibility of irreversible cellular injury due to an antibody antigen reaction has been suggested. The sparing of certain fetuses might be partly dependent on the relative concentration of antigen in the brain. While other tissues also would be involved, their greater reparative capacities than exists in the neuron would militate against permanent injury. The second and more likely possibility would make the cerebral injury entirely secondary to the destruction of the red blood cells during certain periods of fetal life. Thus, only when the ratio of blood destruction to blood formation in the fetus was such as to result in an inadequate supply of oxygen to the developing neuron would permanent injury ensue. This would presuppose red cell destruction at a period in fetal life when the future definitive hematopoietic organ (bone marrow) was inadequate to compensate for the continuing destruction. Later, when this compensation becomes adequate, further neuronal damage would be prevented, although not before a variable degree of injury had already been established. Thus, only in those cases in which maternal antibodies were produced in sufficient concentration relatively early in pregnancy would kernicterus be observed. This concept would agree with the lack of correlation between the severity of the postnatal hemolytic anemia and the occurrence of kernicterus. Finally, the possibility that the products of extensive red cell destruction per se may be injurious to the developing neuron must be considered.

It is to be expected that more patients with kernicterus will survive than heretofore as our knowledge of the treatment of the natal hemolytic anemia expands. The use of Rh negative blood, the appreciation of the relatively large quantity of blood required and the possibility of using separated red cells will function in this direction. Unfortunately, the brain damage cannot be affected by these means. Since concentration of maternal antibodies can be estimated with reasonable accuracy, it is customary, when laboratory facilities are available, to follow the level of maternal antibody formation throughout pregnancy so that premature interruption of pregnancy can be instituted, if the antibody level shows a tendency to rise rapidly. Whether this will result in a reduced incidence of kernicterus is questionable. It is clear that the fetus is exposed to the maternal agglutinins early in pregnancy and that the brain damage is probably well established at a variable period before term. However, reported experience with premature interruption of pregnancy as a prophylactic measure in this respect is too scanty to warrant drawing definite conclusions.

11. Boorman, Kathleen E., and Dodd, Barbara E.: Group Specific Substances A, B, M, N, Rh: Their Occurrence in Tissues and Body Fluids, J. Path. & Bact. **55**: 329 (July) 1943.

SUMMARY

The incidence of incompatible mother-child Rh blood typings was found to be significantly higher in a group of undifferentiated mental defectives than in a control group. This suggests that the cerebral abnormality of some of these undifferentiated defectives is probably related to maternal Rh isoimmunization during pregnancy.

Of the 19 cases in the undifferentiated group in which this etiologic possibility exists, 6 cases were found in which either definite or presumptive evidence of maternal isoimmunization was present. The neonatal history in all 6 of these cases was considered compatible with the diagnosis of erythroblastosis fetalis. In 4 of these children the clinical picture was fairly uniform, including spasmodic increases in muscle tone, choreoathetosis and evidence of cerebellar dysfunction. In 1 case the signs of cerebellar dysfunction dominated the picture. In the remaining case there was no athetosis, while the increased muscle tone or spasticity was constant rather than spasmodic.

In the remaining 13 cases no definite evidence of maternal Rh isoimmunization could be demonstrated, and the clinical picture was nondescript except for the mental defect. While statistical considerations suggest that probably 3 or 4 of these may also be etiologically related to the Rh sensitization mechanism, it was felt that confirmatory evidence, both clinical and serologic, obtainable during the neonatal period and related to the subsequent failure in mental development, would be necessary before definite conclusions could be reached in this respect.

ABSTRACT OF DISCUSSION

DR. STANLEY COBB, Boston: This is a good piece of work along an important and new line of investigation. The results suggest that there is much more work to be done in this field, but these results in themselves are not specific enough to be of much value for clinical diagnosis at the present time. They do open up a vista of possibilities for the prevention of cerebral disease in children with its resultant mental defect and other neurologic aftermaths. Previously this had been a field in which therapy was not known and the outlook was hopeless. Now we may at least try to prevent these things by looking for the Rh factor in the blood of the mother and the child. It would be interesting to extend this investigation to cases of Wilson's disease, for here we have a group of patients with both cerebral and hepatic lesions and it might be that the Rh factor would be important in this disease also. The relation of the liver to the basal ganglions has long been a subject of interest to neurologists, and although the jaundice in these patients described by Yannet and Lieberman was in all probability due to destruction of red cells, yet the liver may also be implicated. In the last war there were some cases in which phosgene gas caused acute atrophy of the liver with kernicterus. It is possible that this approach might be used experimentally and illuminate the subject.

DR. BRONSON CROTHERS, Boston: Dr. Yannet and Miss Lieberman have brought under review a series of cases which can be definitely removed from the discouraging mass of feebleminded individuals for careful study. The clinical picture which results from severe erythroblastosis with cerebral damage is reasonably typical. The children that I have recognized are essentially decerebrate with tonic neck reactions and rigidity with athetosis. They are profoundly defective. The suggestion that there must be many less severe cases should be pursued. The authors make out a case which should be considered by every one who sees young defective children in considerable numbers. It is entirely practicable to collect evidence, and unfortunately the material is readily and continuously available.

DR. HERMAN YANNET, Southbury, Conn.: I am indebted to Dr. Cobb and Dr. Crothers for their discussion and suggestions. The possibility raised by Dr. Cobb that there might be a relationship between kernicterus and Wilson's disease was discussed in an earlier paper (Zimmenman, H. M., and Yannet, Herman: Kernicterus, *Am. J. Dis. Child.* **45**:740, 1933). The striking dissimilarities, especially the times of onset of clinical symptoms in Wilson's disease, make it very unlikely that the two conditions are related. However, Rh investigative procedures could very easily be applied, so that any doubt may be dispelled.

PENICILLIN IN SPINAL FLUID AFTER INTRAVENOUS ADMINISTRATION

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Demonstrable penicillin levels in the cerebrospinal fluid have been reported after intravenous or intramuscular administration only in patients who had inflammatory processes of the meninges [1] or when the penicillin was given by direct instillation.[2] Attainment of significant [3] penicillin activity in the cerebrospinal fluid of patients who did not show evidence of meningeal involvement is not reported in the available literature.

McDermott and Nelson [4] and Mackie,[5] utilizing intramuscular doses as high as 500,000 Oxford units, failed to achieve significant cerebrospinal fluid concentration. Our own efforts, during the past twenty-two months, after intramuscular doses of 20,000, 40,000 and 200,000 units have likewise been unsuccessful. Neymann, Heilbrunn and Youmans [6] recently concluded that the intravenous and intramuscular methods of administration of penicillin were ineffective because "the hematoencephalic barrier cannot be breached."

We are presenting a series of cases in which significant levels of penicillin were obtained in the cerebrospinal fluid by means of the intravenous route of administration.

Massive dose penicillin therapy by continuous intravenous drip is being investigated as a method of treatment of early syphilis the results of which will be the subject of a later report. A group of 162 patients exhibiting clinical evidence of primary or secondary syphilis was the subject of this study. All were dark field positive for Treponema pallidum. Eligibility for treatment was determined on the basis of freedom from detectable pathologic changes of the cardiovascular pulmonary, urinary and hemopoietic systems. Electrocardiograms and 2 meter chest roentgenograms were included in the pretreatment medical survey. Cerebrospinal fluid examinations performed routinely before treatment revealed normal findings in all but 9 patients. There was no clinical evidence of meningeal involvement. Previous investigation [7] revealed abnormal cerebrospinal fluid in 16.4 per cent of 1,380 patients with untreated early syphilis. It was thought that by the intravenous administration of massive amounts the penicillin might surmount the hematoencephalic barrier and circulate through the cerebrospinal fluid system.

The patients received sodium penicillin by the continuous intravenous drip method in amounts ranging from 10 million to 25 million units over a twenty-four hour period. The total amount of penicillin was contained in 1,000 cc. of isotonic solution of sodium chloride.

The administration of penicillin by the intravenous drip technic is known to cause thrombophlebitis; [8] therefore an attempt was made to circumvent this complication by the use of the anticoagulant heparin incorporated in the "Pitkin menstruum." [9] Three hundred mg. of heparin was injected subcutaneously into the anterolateral aspect of the thigh immediately before the institution of penicillin therapy.

The patients were given the intravenous drip by the usual technic utilizing veins of the forearm. The rate of flow of the solution was regulated by means of a pinch clamp to deliver 1,000 cc. of solution continuously over a twenty-four hour period.

The levels of penicillin in the blood and cerebrospinal fluid were determined by the method described by Rosenblatt, Alture-Werber, Kashdan and Loewe [10] at intervals of six hours during the drip procedure and six hours after completion of therapy. All blood specimens were kept in the refrigerator until immediately before setting up the tests, which were run daily. The serums were removed by centrifugation and tested for penicillin activity by a tube dilution technic using Streptococcus pyogenes, strain C-203, group A, as the test organism. The calcium salt of penicillin supplied by the Food and Drug Administration was used as a reference standard.

The specially prepared penicillin utilized in these investigations was supplied by Mr. John L. Smith of the Charles Pfizer and Co. Inc.

Because of lack of space, this article is abbreviated here by the omission of tables giving the penicillin levels in patients receiving 10, 15, 20 and 25 million Oxford units.

From the office of the President of the Chicago Board of Health and the Chicago Intensive Treatment Center, Venereal Disease Control Program, in cooperation with the United States Public Health Service.

Valuable advice was given by Dr. Philip Rosenblatt. Loyal assistance was given by Drs. H. C. McCraney and Lydia Marshak. The work was made possible with the help of a technical group consisting of Elsie Miller, B.A., Ellen Bienfang, R.N., and Mary Gleason.

1. Tee, G. H.: A Case of Meningococcal Meningitis Treated with Penicillin, Lancet **1**:118 (Jan. 27) 1945. Rosenberg, D. H., and Sylvester, J. C.: The Excretion of Penicillin in the Spinal Fluid in Meningitis, Science **100**:132 (Aug. 11) 1944. McDermott and Nelson.[4]

2. Bloomfield, A. L.; Kirby, W. M., and Armstrong, C. D.: A Study of "Penicillin Failures," J. A. M. A. **126**:685 (Nov. 11) 1944. Rosenberg, D. H., and Arling, P. A.: Penicillin in the Treatment of Meningitis, ibid. **125**:1011 (Aug. 12) 1944. Herrell, W. E.; Nichols, D. R., and Heilman, D. H.: Penicillin, ibid. **125**:1003 (Aug. 12) 1944. McCune, W. S., and Evans, J. M.: Intraventricular Penicillin in the Treatment of Staphylococcic Meningitis, ibid. **125**:705 (July 8) 1944. Baird, K. H.: Penicillin Therapy of Pneumococcic Meningitis: Report of a Case with Recovery Following Intraspinal, Intracisternal, and Intraventricular Administration of Penicillin, J. Pediat. **26**:287 (March) 1945. Neymann, Heilbrunn and Youmans.[6]

3. Significant levels for the purposes of this paper are 0.01 to 0.078 unit per cubic centimeter, as reported by McDermott, Benoit and DuBois (Time-Dose Relationships of Penicillin Therapy: III. Regimens Used in Early Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **29**:345 [May] 1945) to be the "effective level" for Treponema pallidum, group A streptococcus and many other organisms.

4. McDermott, W., and Nelson, R. A.: The Transfer of Penicillin into the Cerebrospinal Fluid Following Parenteral Administration, Am. J. Syph., Gonor., & Ven. Dis. **29**:403 (July) 1945.

5. Mackie, T. J.: Personal communication to the authors.

6. Neymann, C. A.; Heilbrunn, G., and Youmans, G. P.: Experiments in the Treatment of Dementia Paralytica with Penicillin, J. A. M. A. **128**:433 (June 9) 1945.

7. Bundesen, H. N.; Bauer, T. J., and Kendell, H. W.: The Intensive Treatment of Gonorrhea and Syphilis, J. A. M. A. **123**:816 (Nov. 27) 1943.

8. Anderson, G. D.: The Treatment of Infections with Penicillin, New England J. Med. **232**:400 (April 5) 1945. Keefer, C. S.; Blake, F. G.; Marshall, E. J., Jr.; Lockwood, J. S., and Wood, W. B., Jr.: Penicillin in the Treatment of Infections: Report of 500 Cases, J. A. M. A. **122**:1217 (Aug. 28) 1943.

9. Loewe, L., and Rosenblatt, P.: A New Practical Method for Subcutaneous Administration of Heparin, Am. J. M. Sc. **208**:54 (July) 1944.

10. Rosenblatt, P.; Alture-Werber, E.; Kashdan, F., and Loewe, L.: A Method for the Determination of Penicillin Levels in Body Fluids, J. Bact. **48**:599 (Nov.) 1944.

A lumbar puncture was performed within thirty minutes of completion of treatment and the penicillin concentration of the cerebrospinal fluid determined.

It was decided, after the first 25 patients had been studied, to determine the level of penicillin in the blood only twice during the period of treatment, at twelve and twenty-four hours after the institution of therapy.

Penicillin was demonstrated in measurable concentration in the cerebrospinal fluid of 126 of the 162 patients (77.7 per cent). These 126 comprised 48 of the 53 (91 per cent) patients who had received over 10 million units of penicillin and 78 of the 109 (71.5 per cent) patients treated with 10 million units of penicillin. The concentration of penicillin ranged from 0.02 to 0.55 Oxford unit per cubic centimeter. Patients receiving 10 or 15 million units showed 0.10 or below with 2 exceptions, and 49.3 per cent of the specimens on the 10 million group reveal 0.02 to 0.03 Oxford unit. The highest level, 0.55 Oxford unit, was obtained for 1 patient on the 25 million unit schedule. The range in levels for the 9 patients with abnormal cerebrospinal fluids was from 0.02 to 0.40 Oxford unit.

No conclusive evidence was established as to the relationship of body weight to levels of penicillin in the cerebrospinal fluid.

There was a direct relationship between the total dosage and the level of penicillin in the cerebrospinal fluid, as shown in the table.

The relationship between the amounts of penicillin in the cerebrospinal fluid and the blood was not clearly established, although some tendency was indicated. Thirty-one patients of the 109 (28.4 per cent) treated with 10 million units had no penicillin activity in the cerebrospinal fluid. Twenty-four of this group (77.4 per cent) had 20 units of penicillin or less in the blood. Seventy-eight (71.5 per cent) patients did have penicillin activity in the cerebrospinal fluid. Thirty-seven (47.4 per cent) of this group had 20 or more units of penicillin in the blood

Concentration of Penicillin in the Cerebrospinal Fluid

Oxford Units per Cubic Centimeter

Total Dose of Penicillin in Million Oxford Units	Maximum	Minimum	Average	Per Cent of Patients Showing Penicillin
10	0.39	0.00	0.029	71.5
15	0.12	0.00	0.048	70.6
20	0.40	0.025	0.043	100.0
25	0.55	0.04	0.213	100.0

An analysis of blood levels taken six hours after treatment was completed showed detectable penicillin in only 7 of 31 patients studied.

COMMENT

Clinical improvement has been observed in the penicillin treatment of the purulent meningitides,[11] neurosyphilis [12] and brain abscess,[13] but there are few studies on the levels of penicillin in the cerebrospinal fluid.

The importance of attaining an effective therapeutic level of penicillin in the cerebrospinal fluid in those diseases in which it is desirable that the drug arrive at the site of the pathologic process cannot be overemphasized.

As the instillation of penicillin directly into the cerebrospinal fluid via lumbar, cisternal or ventricular puncture is technically difficult and often hazardous,[14] the achievement of an effective therapeutic penicillin level by the intravenous method of administration is of prime importance.

Reactions were encountered in some patients during and after treatment consisting of thrombophlebitis, nausea, vomiting and azotemia. These will be presented in detail in a subsequent report. No fatalities occurred and no convulsions or signs of meningeal irritation were observed.

SUMMARY

Patients with early syphilis were given penicillin by the continuous intravenous drip technic in amounts varying from 10 to 25 million units in a period of twenty-four hours.

Significant quantities of penicillin were demonstrated in the cerebrospinal fluid in the majority of the patients.

11. Tee [1] and the references given in full in footnote 2.

12. Nelson, R. A., and Duncan, L.: Acute Syphilitic Meningitis Treated with Penicillin, Am. J. Syph., Gonor. & Ven. Dis. **29:** 141 (March) 1945. Gammon, G. D., and others: Penicillin in Neurosyphilis, J. A. M. A. **128:** 653 (June 20) 1945. Goldman, D.: Treatment of Neurosyphilis with Penicillin, ibid. **128:** 274 (May 26) 1945.

13. Furlow, L. T.: Penicillin as an Adjunct to Surgery in the Treatment of Brain Abscess: Report of 6 Cases, South. M. J. **38:** 312 (May) 1945.

14. Johnson, H. C., and Walker, A. E.: Intraventricular Penicillin: A Note of Warning, J. A. M. A. **127:** 217 (Jan. 27) 1945. Neymann, Heilbrunn and Youmans.[6]

Clinical Notes, Suggestions and New Instruments

ENDOMETRIOSIS CAUSING INTESTINAL OBSTRUCTION

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Endometriosis externa occurs not infrequently. This condition is usually seen involving the oviducts, pelvic peritoneum, rectum and mesorectum.[1] It has also been seen involving the ileum, appendix, cecum, ureter, bladder and skin surfaces particularly in the region of the umbilicus and in old operative scars of the anterior abdominal wall. Green-Armytage [2] reports the general incidence of endometriosis as 8.9 per cent in 1,000 surgical cases.

Endometrial implantation means that there is primary seeding from the site of origin. Endometrial transplantation means that there is secondary embedding from an implant. The case reported here represents endometriosis externa of the implant type.

With the exception of rectum and mesorectum, intestinal contaminations are all derived primarily from the tubal "spill" or secondary rupture of endometrial cysts. Every transplant or implant on a free peritoneal surface becomes a potential center for further transplants.

When a group of endometrial cells settles on a favorable surface, fixation occurs followed by invasion. A small operculum in the peritoneum by which the invasion was made soon closes over and a potential endometrial cavity is formed. These tissues tend to develop their original architecture. A menstruation diapedesis occurs in this potential cavity at the next menstrual epoch, and rupture at any subsequent menstruation is a possibility. Parts of the gastrointestinal tract most susceptible to these transplantations or implantations are the sigmoid, rectum, appendix, cecum and the lower part of the ileum.[1]

Intestinal obstruction as a result of endometriosis has been observed frequently. Most instances, however, are those involv-

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1. Goodall, Robert: A Study of Endometriosis, Philadelphia, J. B. Lippincott Company, 1943.

2. Green-Armytage, V. B.: Endometriomata: The Five Clinical Types, Brit. M. J. **1:** 602 (April 8) 1933.

ing the sigmoid and mesorectum. Relatively few cases of acute complete obstruction have been recorded in the literature. Glenn and Thornton [3] report 2 cases of partial intestinal obstruction of the chronic type due to endometrial implantation.

Masson [4] reports 689 organs of 576 patients with endometriosis. Most of the structures involved were pelvic genital organs. The intestines were involved in 17 instances; of these the colon was involved 14 times, the appendix twice and the ileum once. Keen and Kimbrough [5] did not find the small bowel involved in any of 118 proved cases of endometriosis, nor did Cullen [6] in reporting personal observations over a twenty-five year period. A review of the English literature over a twenty-five year period revealed only 4 cases of endometrial implants involving the small bowel and producing varying degrees of obstruction, none acute. However, the true incidence of endometrial implants in the small bowel is unknown.

This case is worthy of recording because of the short duration of symptoms from the time of onset. Also this patient had an appendectomy performed fifteen years previously, at which time no pathologic state other than acute appendicitis was observed. Furthermore, it represents an instance of acute complete obstruction due to endometriosis which necessitated resection of a part of the ileum.

REPORT OF CASE

A white woman aged 38, first seen by us on Dec. 31, 1944, complained of midepigastric pain, nausea and vomiting.

Her past history was negative except for scarlet fever at 16 years, a submucous resection in 1926, an appendectomy in 1930 and a tonsillectomy in 1931.

Menstruation started at the age of 13. The flow was moderate. There was always slight dysmenorrhea; the cycle was twenty-one to thirty-one days. There were no pregnancies, miscarriages or abortions. No intermenstrual discharge or pain was elicited.

Fig. 1.—Obstruction of small intestine disclosed by barium enema.

She stated that her first attack of pain was on Nov. 19, 1944 at the time of her regular period. This pain was continuous and quite severe. It lasted until her period stopped. For the remainder of November and also during her December period she had no pain. On December 31 she started to menstruate again, and the same pain recurred. She vomited and was somewhat relieved. The pain continued, however, for the full duration of her period. Since this pain was midepigastric and at times radiated to her back and right subscapular region, it was necessary to rule out peptic ulcer and cholelithiasis.

Fig. 2.—Section of ileum, slightly reduced from a photomicrograph with a magnification of 100 diameters.

An upper gastrointestinal series and cholecystogram were negative. Gastric analysis was normal. Antispasmodics and sedation were prescribed during the following intermenstrual period, and the patient was without symptoms. There were no tarry stools, the vomitus was never bloody nor was the patient jaundiced at any time.

On Jan. 27, 1945 the patient began to menstruate. At this time she also developed severe right lower quadrant pain, abdominal distention, nausea and vomiting. It became evident that she was having some sort of small bowel obstruction. Peristalsis was hyperactive with gurgling. Tympanites was present and the pain soon became generalized. The temperature was 100 F., and white blood cells numbered 10,000. Morphine sulfate ¼ grain (0.016 Gm.) hourly was required for relief of pain. A gastrointestinal series with barium enema was performed (fig. 1) and established the diagnosis of small bowel obstruction. Laparotomy was performed by Dr. Deibert as follows:

Under spinal procaine anesthesia a right rectus incision was made. The omentum was found to be adherent to the parietal peritoneum. These were incised and the contents of the abdominal cavity were found to be normal, except for the terminal ileum, which showed what appeared to be a hard constricting band of fibrous tissue about 3 inches from the ileocecal junction. This completely occluded the lumen of the bowel. A resection of the involved portion was done and a side to side anastomosis of the ileum and cecum was performed. Convalescence was uneventful.

Review of histologic sections (fig. 2) by Dr. Read revealed the following:

Diagnosis: Endometriosis of the ileum.

Gross: The specimen was 6 cm. of small bowel. The mucosal surface appeared relatively normal, but there was thickening and distortion of the serosa.

Microscopic: The section was of ileum. The mucosa and submucosa were relatively normal. The muscularis showed hypertrophy and here, but more particularly in the serosa, there were small collections of simple glands surrounded by stroma. There were erythrocytes in the lumen of some of the glands. The lesion was endometriosis of the serosa of the ileum.

3. Glenn, P. M., and Thornton, J. J.: Endometriosis of the Ileum, J. A. M. A. **115**: 520-522 (Aug. 17) 1940.
4. Masson, J. C.: Surgical Significance of Endometriosis, Ann. Surg. **102**: 819 (Nov.) 1935.
5. Keen, F. E., and Kimbrough, R. A., Jr.: Endometriosis: A Review Based on the Study of 118 Cases, J. A. M. A. **95**: 1164 (Oct. 19) 1935.
6. Cullen, T. S.: The Distribution of Adenomyomas Containing Uterine Mucosa, Arch. Surg. **1**: 215 (Sept.) 1920.

COMMENT

In a case of acute intestinal obstruction involving the terminal ileum, the cause was endometriosis. The symptomatology at first suggested cholecystic disease or peptic ulcer. The history was typical of endometriosis, the attacks coinciding with the menstrual periods. As noted, this is an unusual type of complete small bowel obstruction.

2029 Delancey Street.

Council on Pharmacy and Chemistry

REPORT TO THE COUNCIL ON PHARMACY AND CHEMISTRY

Six drug manufacturers interested in thiouracil have cooperated with the Food and Drug Administration to prepare a survey by questionnaire of the toxicity of this drug. The study involved the results of the use of thiouracil in 5,745 cases and was undertaken before the drug became available in interstate commerce. When the survey was completed it was reported to the Council on Pharmacy and Chemistry with a view to informing this body, and through it the medical profession, of the status of thiouracil. The Council warmly commends such cooperation and urges that manufacturers show a similar spirit in other therapeutic problems of common interest. When physicians are supplied with potent drugs they must also be supplied with adequate information concerning their actions, use and dangers.

AUSTIN SMITH, M.D., *Secretary,*

THE CLINICAL TOXICITY OF THIOURACIL

A Survey of 5,745 Cases

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Because of the difficulty of determining from reports in the literature the incidence and severity of the toxic reactions resulting from the administration of thiouracil for the treatment of hyperthyroidism, a survey by questionnaire has been made of 5,745 patients treated by 328 clinical investigators. The results derived from this survey have been analyzed by statistical methods and constitute the basis of this report.

Data obtained by questionnaire are subject to certain inherent errors. Failure to answer a question, misinterpretation of a question and accidental insertion of an incorrect figure are among the sources of error in organizing such statistics. The necessity for arbitrary grouping and condensation of data and the inability to reflect secondary factors influencing the answer to a given question contribute to the errors of analysis. Some of these deviations can be held to a minimum by careful phrasing of the questionnaire and by intelligent interpretation of the answers. In a consideration of the data presented here, therefore, these inherent errors must be borne in mind although accepted statistical methods were used in their organization so as to limit the deviations to an irreducible minimum. It is believed nevertheless that the trends disclosed and the conclusions reached as a result of this survey are correct, even though the statistics are subject to the errors mentioned.

Miss Lila Knudsen and Mr. Pete James of the Food and Drug Administration tabulated the data and supplied the statistical analysis.
From Drug Division, Food and Drug Administration, Federal Security Agency, and the Medical Departments of Lederle Laboratories, Abbott Laboratories, Eli Lilly & Co., E. R. Squibb and Sons, Parke Davis & Co., and the Upjohn Company.

CLINICAL MATERIAL AND THERAPEUTIC APPRAISAL

The material which forms the basis for this report is derived from large clinics, from small clinics and from individual practitioners. Some of the patients were subjected to the closest scrutiny, which included repeated and extensive laboratory studies; others were followed in less detail.

Many patients were hospitalized, but many were ambulatory during treatment. Despite these variations, it is believed that the results of this survey represent closely those which may be expected when thiouracil becomes generally available to all physicians.

Since the clinical safety of any potent therapeutic agent should be appraised only in the perspective of its therapeutic usefulness, certain information regarding the value of thiouracil in the treatment of hyperthyroidism was collected. Published reports leave little doubt that in most instances the administration of thiouracil can bring about a remission of the hyperthyroid state. Its usefulness in other conditions associated with derangements of thyroid activity has not been completely evaluated.

This survey revealed that thiouracil is effective against all types of hyperthyroidism whether these are represented by diffuse or by nodular goiters and regardless of the number of nodules. Thiouracil may also be of value in the treatment of acute thyroiditis, although data on this condition are scanty. The drug has been tried and found to be of no value in simple goiter. It has been tried without any useful effect in conditions with related symptomatology but where no hyperthyroidism exists.

An attempt was made to determine what, if any, factors contributed to a successful outcome of thiouracil therapy. The incidence of failure to respond to thiouracil has been correlated with such factors as dose, duration of treatment, and whether iodine therapy had been used prior to thiouracil. Only those cases in which thiouracil was used for treatment of hyperthyroidism are considered and failures directly attributable to toxic reactions are not included in the accompanying tabulations.

A correlation could not be established between either the initial dose or the maintenance dose and the incidence of failure. The number of cases in which 0.1 Gm. per day was given as an initial dose is too small to be statistically significant. The majority of investigators used either 0.4 Gm. per day or 0.6 Gm. per day, and since the results are as satisfactory at the lower figure as at the higher, it would appear preferable to recommend 0.4 Gm. per day as the initial dose.

Clinical experience has shown that thiouracil should be administered in divided doses throughout the twenty-four hour period. Administration only once a day is generally followed by poor results. For best results it is suggested that the total daily dose be divided into three or four parts which are administered at equal intervals during the waking hours.

It has been a common observation that a clinical response to thiouracil may not be seen for several weeks

after treatment is started. In this survey there were 209 failures reported in which the duration of treatment was given. Chart 1 shows that the incidence of successful treatment increased as the duration of treatment was prolonged. No explanation is apparent for the low incidence of success at six months, but the figure for

TABLE 1.—*Failures of Thiouracil Therapy in Relation to Initial Dose of Thiouracil*

Initial Dose, Gm. per Day	Total Cases	Failures	
		Number	Per Cent
0.1	35	0	0.0
0.2	268	9	3.4
0.3	187	12	6.4
0.4	669	30	4.5
0.5-0.6	3,448	135	3.9
0.7-0.9	504	32	6.3
1.0 or over	622	31	5.0
Total.....	5,733	249	4.3

thirteen months was derived from too small a number of patients to be significant. To emphasize the desirability of prolonged treatment before classifying a lack of response as a failure, it was observed that in 34 per cent of those patients reported as failures, treatment was discontinued before the eighth week.

It is not uncommon for a patient to show no response to thiouracil in the first four to eight weeks of treatment if iodine had previously been administered or if the gland was large and soft. It is noteworthy, therefore, that of the 71 failures which occurred during the first eight weeks 70 per cent had had iodine therapy prior to thiouracil treatment. This suggests that some might have responded satisfactorily if the medication had been continued for longer periods.

It was not possible to obtain reliable figures on the incidence of remissions induced by thiouracil. By remission is meant absence of symptoms and a basal metabolic rate within the normal range after the drug was discontinued. The majority of investigators did not terminate treatment except in those cases in which thyroidectomy was performed; hence there is no way to determine the duration of remission without the drug. It is evident, however, that of the 1,236 remissions reported in the series 33.7 per cent had relapsed at the time of inquiry. Remissions as long as a year or more have been reported, but the average relapse occurred in

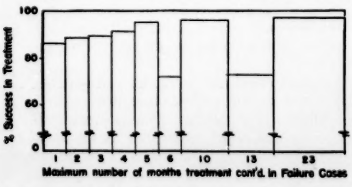

Chart 1.—Relation of satisfactory response to thiouracil to duration of treatment.

about twenty weeks. Hence, until more is known regarding the conditions influencing both remission and relapse, it is futile to speculate on this problem.

TYPE AND INCIDENCE OF TOXIC REACTIONS

The principal toxic reactions observed following medication with thiouracil are granulocytopenia, leukopenia, drug fever and dermatitis. At least twenty-seven other reactions were recorded, of which only eight were observed in more than 2 cases. This suggests that most of the reported side reactions other than those specifically named or the eight mentioned later were not related to thiouracil medication.

Twenty-eight investigators reported that the drug occasionally produced nausea sometimes accompanied by dizziness, headache or abdominal cramps. Parotitis and joint pains have each been reported by seven investigators. Purpura was reported by six, jaundice by four, diarrhea by four, thyroiditis by three and secondary anemia by three investigators. Edema, particularly of the extremities, has been mentioned by several investigators as occurring during therapy. It is not clear in all cases that this was due either directly to the drug or to the rapid metabolic and circulatory changes resulting from correction of the hyperthyroidism.

The eight complications of low incidence may or may not be related to administration of thiouracil, since these reactions did not occur with a frequency greater than expected in 5,000 persons selected at random and observed for a period of six months to a year. It is recommended, however, that these complications should

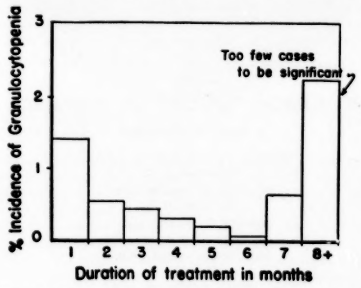

Chart 2.—Relation of incidence of granulocytopenia to duration of treatment.

be watched for, since it cannot definitely be proved that the drug was not the responsible agent.

In the series studied in this investigation, 752 cases in which one or more side reactions occurred were reported. This represents an incidence of 13.1 per cent. These complications were considered by the investigators as severe enough to warrant discontinuance of therapy of 452 patients, or 60.1 per cent of those showing some side reaction.

GRANULOCYTOPENIA

Since the most serious complication of thiouracil therapy appears to be granulocytopenia, it was pertinent to inquire concerning the frequency of this complication and whether its occurrence could be correlated with the dose, duration of treatment or other factors. A diagnosis of granulocytopenia was accepted if the total white count was below 4,000, the granulocytes particularly diminished and associated with sudden onset and acute symptoms such as fever, sore throat, prostration and malaise. Unfortunately not all cases of apparent malignant granulocytopenia are clearly distinguishable from simple neutropenia, particularly in the early stages. The investigators reported 168 cases of granulocytopenia, but only 142 of these could clearly be classed as the frank malignant type. The remaining 26 cases appeared to be early cases or atypical simple leukopenia

with neutropenia, but because the investigators classed them as granulocytopenia they are included as such in these tabulations. The 142 cases of granulocytopenia represent an incidence of 2.5 per cent of this complication and accounted for about 22 per cent of all toxic reactions.

TABLE 2.—*Incidence of Granulocytopenia During Thiouracil Therapy in Relation to Initial Dose of Drug*

Initial Dose, Gm. per Day	Total Cases	Granulocytopenia	
		Number of Cases	Per Cent of Total Cases
0.1-0.4	1,159	33	2.8
0.5-0.6	3,448	109	3.2
0.7-0.9	504	14	2.8
1.0 and over	612	12	2.0

It can be seen from table 2 that there is no significant relationship between the incidence of granulocytopenia and the dosage of thiouracil. There was, however, a very clear relationship between the duration of treatment and the occurrence of this complication. Chart 2 shows that the incidence of granulocytopenia was greatest during the first four weeks of treatment and declined progressively thereafter. The incidence of this complication in the first month of treatment was 1.4 per cent, and more than one half of all the cases occurred during this period. Seventy per cent of the cases of granulocytopenia occurred by the end of the eighth week of treatment. No apparent explanation was found for the high incidence during the seventh month of treatment, but it is suggested that some patients may have lapsed in treatment at this time, and it is generally believed that resumption of therapy after such a lapse may predispose the patient to this complication.

One case of agranulocytosis was reported to have occurred during the fifty-sixth week of treatment, and 1 case, not included in these tabulations, was reported to have occurred six months after discontinuance of treatment. The first case may also have occurred after a temporary discontinuance of therapy.

There were twenty-one deaths, all attributable to agranulocytosis, establishing a mortality rate of 0.4 per cent for the entire series and a case fatality rate for agranulocytosis of 14 per cent. From the information available in the literature and that obtained in this survey, the most effective treatment of agranulocytosis due to thiouracil appears to be the parenteral administration of massive doses (500,000 units per day) of penicillin, and some investigators suggest repeated transfusions of small amounts (200 to 300 cc.) of whole blood. However, there are some who are not in favor of unnecessarily frequent blood transfusions because it has been shown statistically that repeated transfusions increase the risk of transfusion reaction. There is no satisfactory evidence that pantothenic acid, pyridoxine, folic acid, vitamins or pentnucleotide influence the outcome of this disease or aid in preventing such reactions. The most important factor in the control of granulocytopenia resulting from thiouracil therapy appears to be discontinuance of therapy at the earliest sign of this complication and prompt institution of vigorous treatment. It is imperative that the patient be instructed to stop the drug and report immediately to the physician if symptoms such as sore throat, fever, coryza or malaise are noted. The value of repeated blood counts is emphasized by the fact that 1 patient was found to have a complete absence of granulocytes three days before any symptoms developed.

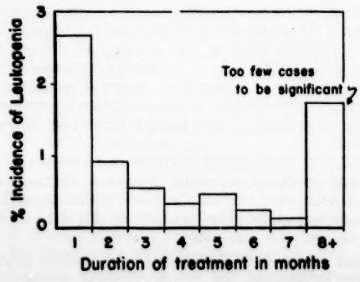

Chart 3.—Relation of leukopenia to duration of treatment.

LEUKOPENIA

One third of all the reported toxic reactions consisted of a leukopenia. In many instances it was difficult to distinguish between a simple leukopenia and an early malignant granulocytopenia. In this survey a designation of simple leukopenia was made when the total white blood cell count was below 4,000, the differential count was relatively normal and the patient showed no subjective symptoms. It may be questioned whether all the cases of leukopenia reported were actually caused by thiouracil administraion, since hyperthyroidism itself predisposes toward a leukopenic state. However, there seems to be a clear relationship between the administration of the drug and the onset of this complication, and it is felt that any reduction in total white count while the patient is under treatment with thiouracil should be viewed seriously.

TABLE 3.—*Incidence of Leukopenia in Relation to Initial Dose of Thiouracil*

Initial Dose, Gm. per Day	Total Cases	Leukopenia Cases	Per Cent Incidence
0.1-0.4	1,159	58	5.0
0.5-0.6	3,448	119	3.5
0.7-0.9	504	44	8.7
1.0 and over	622	30	4.8

Of the 251 cases of leukopenia reported in this series, 234 lend themselves to fairly detailed analysis. This complication had an overall incidence of 4.4 per cent. From table 3 it may be seen that dosage bore no relationship to the incidence of leukopenia. The relationship between incidence and duration of treatment is shown in chart 3 and resembles closely that of granulocytopenia. The incidence of leukopenia in the first four weeks was 2.7 per cent, and 60 per cent of all these cases occurred during this period. Seventy-five per cent had occurred by the end of eight weeks and 95 per cent by the end of six months.

In a number of cases in which leukopenia developed, administration of thiouracil was continued and in nearly half of these a gradual return of the white cell count to normal limits was observed. No reliable figures were obtained on the seriousness of this complication, and it appears that in some instances it may not be harmful to the patients. However, since it cannot be predicted which case may or may not have a serious prognosis, it would seem imperative either to discontinue treatment or have the patient report to the physician at

frequent intervals for repeated examinations of the blood. Hospitalization of the patient should be considered if examination reveals a decided reduction in granulocytes.

This precaution is further emphasized by the fact that although 121 patients developed granulocytopenia without a previous leukopenia, and 198 patients developed a leukopenia which did not pass into a granulocytopenia, 47 patients had both complications. If these two complications were to occur in the same individual purely on the basis of chance, it would be expected that these would occur in not more than 7 or 8 patients in a series of the size studied. The actual incidence was six and one-half times the expected incidence, and this difference, when tested by statistical methods, was found to be highly significant ($P<0.001$). This suggests that all patients who develop a leukopenia during therapy should be closely watched.

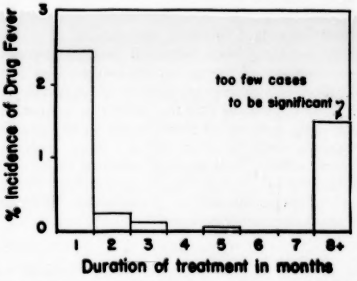

Chart 4.—Relation of drug fever to duration of treatment.

DRUG FEVER

Drug fever is a reaction not infrequently seen following therapy with a wide variety of substances. It is not surprising, therefore, that this complication was reported in 154 individuals following thiouracil therapy. The incidence of this reaction amounted to 2.7 per cent of all cases and accounted for 20.5 per cent of all toxic reactions. By reference to table 4 it is evident that dosage did not influence the incidence of this reaction. Furthermore, this reaction usually occurs early in the course of therapy, as is shown in chart 4.

TABLE 4.—*Incidence of Drug Fever in Relation to Initial Dose of Thiouracil*

Initial Dose, Gm. per Day	Number of Cases	Cases with Drug Fever	Per Cent Incidence
0.1-0.4	1,159	37	3.2
0.5-0.6	3,448	86	2.5
0.7-0.9	504	10	2.0
1.0 and over	622	21	3.3

Thirty per cent of these reactions occurred in the first week of therapy and 85 per cent had occurred by the end of the fourth week. Nearly 10 per cent of the cases of drug fever were observed in the first forty-eight hours, and, if the patient was retested with the drug, fever usually occurred in less than twelve hours. An interesting observation made by several investigators was that when drug fever occurred early in therapy it was usually a more severe reaction, with temperatures as high as 106 F. reported in some instances. In those instances in which the fever was seen during the later stages of therapy, the temperature seldom exceeded 102 F. and the entire reaction was of a milder nature. Since a fever is part of the syndrome of agranulocytosis, any patient receiving thiouracil who develops a fever should be examined immediately and white blood cell and differential counts should be obtained in order to rule out agranulocytosis before classifying the fever as a temperature reaction only.

SKIN REACTIONS

The skin reactions which occurred during thiouracil therapy were varied and usually of a mild nature. One hundred and eighty-nine instances of these complications were observed, an incidence of 3.3 per cent. One fourth of the adverse reactions from thiouracil were skin reactions. The frequency of the various types of skin reaction are given in table 5. As might be expected, dosage had no influence on the incidence, and although there was some tendency for the reactions to occur early in treatment, particularly if other complications occurred in the same patient, the relationship between duration of treatment and incidence was not as striking as that seen with the other complications.

TABLE 5.—*Skin Reactions from Thiouracil Therapy in 5,745 Patients*

	Cases
Urticaria	64
Papular rash	37
Morbilliform rash	23
Erythema	18
Macular rash	17
Acneform rash	3
Pruritus	3
Edema of legs	1
Unspecified dermatitis	23

TABLE 6.—*Opinions on Relative Safety of Thiouracil*

Is the incidence of toxic reactions to thiouracil greater or less than complications of present methods of treating hyperthyroidism?

Answer	Per Cent of Investigators
Less	78.6
Greater	4.2
No opinion	17.2

Although none of the skin reactions were reported as serious, the occurrence of urticaria cannot be regarded as an innocuous reaction. In the case of the sulfonamides such reactions have frequently been associated with more severe complications; hence it would seem advisable to discontinue thiouracil therapy or proceed with great caution if the patient shows an allergic response.

Because of relatively high incidence and severity of the toxic reactions following thiouracil therapy, an attempt was made to poll the investigators regarding their opinions of the relative safety of this drug. The following question was asked:

In your opinion is the incidence of toxic reactions greater than the incidence of bad results (including postoperative thyroid crisis, injury to recurrent laryngeal nerve, parathyroid tetany and other operative complications; uncontrolled or fatal thyrotoxicosis in patients in whom operation is inadvisable or contraindicated) seen with other methods of treatment?

The answers to this question are summarized in table 6. It is apparent that the large majority of those who have had experience with thiouracil feel that it

offers a definite advantage over present methods of treatment of hyperthyroidism from the standpoint of safety.

SUMMARY AND RECOMMENDATIONS

On the basis of this survey covering the experience of 328 investigators in 5,745 cases, the following recommendations appear justified:

1. Thiouracil is effective in the management of thyrotoxicosis and possibly thyroiditis.

2. Thiouracil is of no value and should not be used in other derangements of thyroid activity or in conditions not associated with hyperthyroidism.

3. More information should be secured concerning the induction of remissions by thiouracil and the factors affecting the permanence of these remissions.

4. At present the optimum dosage schedule appears to be 0.4 Gm. per day, in divided doses initially, and after the symptoms are controlled or the basal metabolic rate is within the normal range the dose should be reduced to 0.1 or 0.2 Gm. per day. More information is needed on the effectiveness of lower doses.

5. On the basis of the available information, it can be recommended only that thiouracil be used for preoperative treatment or for those patients for whom operation is contraindicated. The wisdom of depending on thiouracil as a substitute for operative procedure can be determined only by following the results of investigations carried on for longer periods.

6. Many patients, particularly those who have received previous iodine therapy, do not respond immediately to thiouracil therapy; hence medication should be continued for at least thirty days, or, for a patient to whom iodine has been administered, for sixty to one hundred days, before concluding that no response to thiouracil is possible.

7. Approximately 13 per cent of all cases can be expected to show some adverse reaction to thiouracil therapy.

8. The most frequent and severe complications of thiouracil therapy are granulocytopenia, leukopenia, drug fever and dermatitis. The appearance of jaundice, purpura and anemia has been reported and should be watched for and, if observed, calls for careful evaluation of the clinical condition of the patient before thiouracil therapy is resumed.

9. Granulocytopenia occurs in about 2.5 per cent of cases and is the most serious complication of thiouracil therapy. This reaction tends to occur in the early weeks of treatment, and 80 per cent of the cases were seen by the twelfth week of therapy. No relationship to the dose of thiouracil was apparent. Treatment of this complication should consist of massive doses of penicillin (500,000 units per day).

10. Leukopenia had an incidence of 4.4 per cent, seen early in treatment, 75 per cent occurring in the first eight weeks but not related to dosage. More information is needed on the relationship between leukopenia and granulocytopenia.

11. Drug fever had an incidence of 2.7 per cent, seen very early in treatment, 85 per cent occurring in the first four weeks but not related to dosage. Reactions occurring early tended to be more severe than those occurring late in treatment.

12. Skin reactions had an incidence of 3.3 per cent. Urticaria was the most common, but a wide variety of other dermatoses were seen. None were deemed serious, but caution is advised in continuing therapy in the presence of these complications.

13. Three fourths of the investigators were of the opinion that the incidence of adverse reactions of thiouracil was less than the incidence of complications from present methods of treatment.

14. It should be emphasized that patients receiving thiouracil therapy should be carefully watched, especially during the first twelve weeks of therapy. Patients should be instructed to report immediately to their physician if any adverse symptoms such as sore throat, fever, coryza or malaise are experienced.

15. Since the mild and the juvenile types of hyperthyroidism can frequently be controlled adequately by iodine therapy alone, thiouracil should not be used for these patients unless the safer form of therapy proves ineffective.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

CONTRACEPTIVE JELLIES AND CREAMS (See New and Nonofficial Remedies, 1945, p. 355).

The following article has now been accepted:

HOLLAND-RANTOS CO., INC., NEW YORK

U. S. trademark 213,756.

Koromex Jelly: A water soluble jelly formed from tragacanth and gum acacia having a p_H of 4.6, prepared from the formula:

	Per Cent
Boric acid	2.0
Oxyquinoline benzoate	0.02
Phenylmercuric acetate	0.02
Glycerin	10.0
Gum acacia	0.6
Tragacanth	2.5
Perfume	0.015
Butyl parahydroxybenzoate as preservative	0.02
Water	100

Actions and Uses.—See article Contraceptive Jellies and Creams.

Dosage.—5 cc.

SYRINGE APPLICATORS FOR CONTRACEPTIVE JELLIES AND CREAMS (See New and Nonofficial Remedies, 1945, p. 357).

The following article has been accepted:

HOLLAND-RANTOS CO., INC., NEW YORK

Koromex Vaginal Applicator: A transparent plastic tube threaded at the blunt, intravaginal end, to screw onto tubes of Koromex Jelly to permit filling by compression of the tube. The full capacity is 5 cc., the recommended dose.

ACETARSONE (See New and Nonofficial Remedies, 1945, p. 235).

The following dosage form has been accepted:

ALLEN LABORATORIES, INC., PALMER, MASS.

Allen Brand Tampon with Acetarsone (Stovarsol): A lightly compressed stitched tampon of absorbent cotton, coated with 0.1 Gm. of powdered acetarsone, to which is attached a tablet consisting of acetarsone 32 mg. in a tablet base composed of lactose, dextrose, boric acid and starch with a small quantity of sodium bicarbonate and tartaric acid to aid disintegration.

Actions and Uses.—(See article on Acetarsone.)

Dosage.—Intravaginally, one tampon tablet every other day or daily, followed by a mildly acid douche after a third treatment or after a week's treatment, has been reported to give satisfactory results.

THIAMINE HYDROCHLORIDE (See New and Nonofficial Remedies, 1945, p. 610).

The following dosage form has been accepted:

FREDERICK STEARNS & CO., DETROIT

Tablets Thiamine Hydrochloride: 3 mg.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, FEBRUARY 9, 1946

NONTUBERCULOUS PULMONARY CALCIFICATION

Although pulmonary calcification has been generally interpreted as evidence of healed tuberculosis, we recognize now that this disease is not the only important cause of such lesions. Recent epidemiologic studies have shown that a large proportion of persons with pulmonary calcification have negative tuberculin reactions. Lumsden and his associates [1] concluded, after a careful epidemiologic study of Coffee County in southwestern Alabama and Giles County in south central Tennessee, that skin testing with any of the tuberculosis preparations available, as a sole means of establishing an epidemiologic index or rate of incidence of tuberculous infection in a community or in a region, is of doubtful value or definitely futile. Smith [2] suggested that the area of high prevalence of pulmonary calcification and tuberculin negative reactors corresponds with the endemic area of histoplasmosis. Palmer [3] found in a study in which 3,000 nurses in Detroit, Kansas City, Minneapolis and Philadelphia were given intradermal tuberculin and histoplasmin tests and chest roentgenograms that (*a*) mild, probably subclinical, infection with Histoplasma capsulatum (or an immunologically related organism) is widely prevalent in certain states and relatively infrequent in others; (*b*) in general those states in which the frequency of reactions to histoplasmin is high are those in which pulmonary calcification is also high and (*c*) a high proportion of the pulmonary calcifications observed in roentgenograms of tuberculin negative persons is due not to tuberculosis but probably to histoplasmosis.

Christie and Peterson [4] studied a group of 181 children from a children's home in Williamson County, Tenn. Forty-five, or 24.9 per cent, of these reacted to tuberculin; 133, or 73.5 per cent, reacted to histoplasmin, and 79, or 43.6 per cent, had pulmonary lesions interpreted as calcifications. Almost twice as many children had calcification as were tuberculin positive. Positive reactions to histoplasmin were three times as common as positive reactions to tuberculin. Among the youngest group, 41.7 per cent of those under 5 years gave positive reactions to histoplasmin. None of the children under 5 years of age reacted positively to 0.1 mg. of tuberculin. The reactivity to histoplasmin occurred at an earlier age than the appearance of calcium in the lungs or reactivity to tuberculin. Apparently pulmonary calcification occurs less commonly in relation to tuberculin sensitivity than in relation to histoplasmin sensitivity. Of the 78 children with pulmonary calcification 25, or 32 per cent, reacted to 1 mg. or less of tuberculin. There were 53 children who did not react to tuberculin, more than twice as many as did react. Of the whole group 68, or 87.2 per cent, reacted to histoplasmin.

The studies by Gass and his associates and by Lumsden and his associates showed that there is a much greater prevalence of this phenomenon of pulmonary calcification in persons who are not sensitized to tuberculin in the area of the eastern slope of the Mississippi River basin and the adjacent states of the western slope south of Iowa than in the rest of this country. In this general area the overall prevalence of pulmonary calcification varied from 27 per cent in Ohio to 83 per cent in Tennessee. Of these calcified lesions only from 10 to 50 per cent were explainable on the basis of tuberculin sensitivity. Twenty-four to 45 per cent of the children showed pulmonary calcification without tuberculin allergy.

The observations of Gass and his associates [5] on the development of pulmonary calcification while the children were under observation, and its occurrence without showing tuberculin sensitivity during that period, is highly significant. It seems incredible that tuberculin sensitivity could develop and disappear in periods as short as two years. This observation offered the first substantial evidence that some infection other than tuberculosis might be the cause of this widespread unexplained calcification.

These observations, considered together with certain known facts regarding the distribution of fatal cases of histoplasmosis, suggest the possible etiologic relationship between nontuberculous benign pulmonary calcifications and a benign form of histoplasmosis. The conclusions depend largely on determination of the specificity of the histoplasmin reaction, for which only indirect evidence has been presented. With antigens derived from fungi, there is a possibility of crossed immunologic response to coccidioidin and an antigen derived from Haplosporangium.

1. Lumsden, L. L.; Dearing, W. P., and Brown, R. A.: Questionable Value of Skin Testing as a Means of Establishing an Epidemiologic Index of Tuberculous Infection, Am. J. Pub. Health **29**: 25 (Jan.) 1939.

2. Smith, C. E.: Coccidioidomycosis, M. Clin. North America, May 1945, p. 790.

3. Palmer, C. E.: Nontuberculous Pulmonary Calcification and Sensitivity to Histoplasmin, Pub. Health Rep. **60**: 513 (May 11) 1945.

4. Christie, Amos, and Peterson, J. C.: Pulmonary Calcification in Negative Reactors to Tuberculin, Am. J. Pub. Health **35**: 1131 (Nov.) 1945.

5. Gass, R. S., and others: Pulmonary Calcification and Tuberculin Sensitivity Among Children in Williamson County, Tenn., Am. Rev. Tuberc. **47**: 379 (April) 1943.

BIOLOGIC WARFARE

Biologic warfare was a potential menace throughout World War II. Biologic warfare is defined as the use of bacteria, fungi, viruses, rickettsias and toxic agents from living organisms to produce death or disease in men, animals or plants. Between World War I and World War II many came to believe that this type of warfare was possible. Late in 1941 the National Academy of Sciences was requested to survey the current situation and future possibilities. Following a period of development, under the administration of War Research Service, the main responsibility for the program was carried by the Chemical Warfare Service of the Army; at the peak nearly 3,900 persons were devoted to this work, including nearly 1,000 Navy personnel and nearly 100 civilians. The parent installation was Camp Detrick, at Frederick, Md., and there were other facilities in Mississippi, Indiana and Utah.

As a result of these efforts adequate defenses against a potentially dangerous method of warfare were devised, and the possibility of surprise was forestalled. Apart from the military objectives much information of great value for human welfare was obtained. Unique facilities were established for research and experimentation on pathogenic agents on a scale never before possible.

Of the more important accomplishments of especial medical interest were (*a*) development of methods for the rapid and accurate detection of minute quantities of disease producing agents, (*b*) significant contributions to knowledge of the control of airborne disease producing agents, (*c*) production and isolation, for the first time, of a crystalline bacterial toxin, which has opened the way for the preparation of a more highly purified immunizing toxoid, (*d*) development and production of an effective toxoid in sufficient quantities to protect large scale operations should this be necessary, (*e*) significant contributions to knowledge concerning the development of immunity in human beings and animals against certain infectious diseases and (*f*) important advances in the treatment of certain infectious diseases of human beings and animals, and in the development of effective protective clothing and equipment. Steps are being taken to permit the release of such technical papers and reports as may be published without endangering the national security.

Unlike the development of the atomic bomb and other secret weapons during the war, the development of agents for biologic warfare is possible in many countries, large and small, without vast expenditures of money or the construction of huge production facilities. Preparations for biologic warfare could proceed in many countries, perhaps under the guise of legitimate medical or bacteriologic research. For these reasons, supported by the fact that both Germany and Japan are known to have been engaged in activities looking toward biologic warfare, it seems imperative to continue investigations in this field on a scale sufficient to provide an adequate defense. Moreover, new benefits to medicine may be anticipated.

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THE OFFICE OF CORONER

The dubious distinction of having created the institution of the coroner is oftenest accredited to Alfred, surnamed The Great, king of the West Saxons. The original coroner watched for the emoluments accruing to the crown in peculiar circumstances; he inquired into wrecks at sea and secured the flotsam to England, looked into all treasure trove and investigated unusual deaths that the exchequer might not be deprived of the forfeiture of felons. The office of coroner was therefore that of a scavenger; unfortunately an occasional coroner today seems to function in a similar manner.

Sixty-nine years ago the legislature of the state of Massachusetts abolished the office of coroner and substituted a system of medical examiners. The legislative act was prompted by public outcries following inefficient investigation of a peculiarly atrocious crime. In 1915, after prolonged investigation by the commissioner of accounts, the city of New York also abolished the coroner's system and adopted that of the medical examiner. The county of Essex in New Jersey followed.

Wherever the coroner exists in this country his privileges are exceedingly elastic. He may issue subpenas, empanel juries and administer the oath to jurors in order to prosecute inquiry into sudden, violent or suspicious death, no matter how staggering the attendant technical problems may be. He may make or direct postmortem examinations, conduct or institute chemical, bacteriologic and microscopic investigations and, in short, perform the offices of a pathologist. The extent to which the city of New York had previously made provision for the fulfilment of the scientific and quasi-judicial duties of the coroner is indicated by the fact that the post was occupied at various times by a bricklayer, a shoemaker, a carpenter, a stone mason, a plumber, a butcher and an undertaker. The medical responsibilities of the office were delegated to physicians distinguished, with a solitary exception, by political preferment rather than by scientific ability.

The successful conduct of the medical examiner's office is not necessarily limited to thickly populated districts. In the vast territorial expanse covered by the Royal Mounted Police the office of medical examiner, fashioned after the New York City system, functions admirably. In most parts of the United States the office of the coroner continues to exist. Is it not time that our governments modernized their procedures by eliminating this ancient and far too often dishonorable office?

INCOME TAX CREDIT FOR CHARITY PRACTICE OF PHYSICIANS

The value of the services rendered annually by physicians of this country in the treatment of the indigent sick for which they receive no compensation has been estimated as in excess of $300,000,000. Recognition of this tremendous contribution made by physicians for the public good is reflected in a bill, H. R. 5296, introduced in the Congress January 30 by Representative Clare Boothe Luce of Connecticut. The measure provides that physicians, surgeons and dentists, commencing with the taxable year 1946, shall be allowed an additional credit as a deduction on their income tax equal in terms of percentages to that portion of their time each year which is devoted to charity, free clinic work and public research work. The Commissioner of Internal Revenue will prescribe by regulation, it is contemplated, the method of computing such time and the proof which shall be required in substantiation.

At the time the bill was introduced, Representative Luce had inserted in the *Congressional Record* a statement embodying the justification for her sponsorship of this legislation. In connection with the many proposals being made for various kinds of governmental control of medicine, she said:

> None of these proposals is a logical development of the American system of recognizing, promoting and rewarding individual choice and achievement. In our earlier history pioneer medicos were rewarded for their frequently ill paid devotion by a very special place in the community, high respect from their fellow citizens and patients, and payment in lovingly prepared delicacies where cash was scarce. Those times have largely vanished. To become a doctor, a surgeon, a dentist now requires some eight or nine years of unremunerative and expensive schooling. Until he has completed all this, usually by the time he is 29 or 30, the doctor cannot even begin to earn his own bread and salt, much less begin to repay himself for the costs of learning his profession.

After referring to the fact that all reputable physicians give a considerable portion of their time to the treatment of patients who are unable to pay for the services in any way except by gratitude, the statement continues:

> Surveys as to the amount of these unpaid services indicate that the percentages range from around 30 to 45 of all treatments given. This is a direct contribution on the part of the physician, surgeon or dentist to the public welfare. In addition are the hours spent without pay in public research work, on hospital boards and on boards of charitable organizations. All this must be chalked up to professional devotion, since it results in no return and often requires the practitioner to lengthen his working day to fifteen or sixteen hours or more in times of epidemic. There are no limits possible on a doctor's working day.

Because of the facts so well set forth in her statement, Representative Luce believes that the recognition contemplated by her bill is fully justified. This measure is pending before the House Committee on Ways and Means, where, it may be assumed, it will be given consideration by the committee in connection with its program to revise the income tax law.

Current Comment

COMBINED FEVER-PENICILLIN THERAPY

In 1944 Eagle and his associates [1] of Johns Hopkins Hospital showed that the spirocheticidal action of penicillin increases with the temperature in the range 8-40 C. Using five different strains of spirochetes, they found that the percentage of organisms surviving after twenty-four hours at 8, 22-23, 32-33, 36-37 and 39-40 C. was 100, 10, 1, 0.2 and 0.02 respectively. These results were independent of the concentration of penicillin in the range 0.25 to 250 units per cubic centimeter. In their opinion the difference between the results obtained at 37 C. and at 40 C. is sufficiently great to suggest the use of artificially induced fever in conjunction with penicillin in the treatment of syphilis. They believed that such a combined therapy might make it possible to reduce the total dosage, shorten the duration of treatment or do both. Similar effects of hyperthermia on the bactericidal action of penicillin were subsequently reported by Lee and Foley [2] of the Wallace Laboratories, New Brunswick, N. J. In a typical experiment they showed that at 37 C. 1.5 units of penicillin per cubic centimeter of rabbit serum reduced the viable percentage of Staphylococcus aureus 75 per cent by the end of four hours. At 39 C. the viable count was reduced by 83 per cent and at 42 C. by 96 per cent. In control tests without penicillin there was as much as a four hundredfold increase in the bacterial count by the end of the same period. While Lee does not formally recommend combined fever and penicillin therapy in staphylococcic infections, such a combination would be a logical application of his data.

COOPERATIVE STUDIES ON THIOURACIL

Elsewhere in THE JOURNAL (pages 315 and 343) are two clinical communications on the results of cooperative studies on the toxicity of thiouracil, a new drug for the treatment of thyrotoxicosis. The studies should clearly define the toxicity of this drug, which is now available in interstate commerce. Only by careful use can thiouracil be expected to serve beneficially in modern chemotherapy. Moore's report offers the joint experience of eleven clinics in the United States and one in England; it is not intended as an appraisal of the usefulness of thiouracil. The statement by Van Winkle and his associates is the result of information gathered by questionnaire by six drug manufacturers interested in the distribution of thiouracil. This statement has been submitted as a report to the Council on Pharmacy and Chemistry and presents a new and commendable peak in cooperation. Both papers are excellent examples of the value of pooling information and should serve as guides for the future when other new drugs appear on the medical horizon under a cloud of uncertainty.

1. Eagle, Harry, and Musselman, Arlyne D.: J. Exper. Med. **80:** 493 (Dec.) 1944.
2. Lee, S. W., and Foley, E. J.: Proc. Soc. Exper. Biol. & Med. **60:** 133 (Oct.) 1945.

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MEDICINE AND THE WAR

ARMY

GENERAL KIRK AWARDS FIVE OFFICERS LEGION OF MERIT

Five Legion of Merit Awards were recently presented by Major Gen. Norman T. Kirk, Surgeon General of the Army, to Col. James E. Ash, director of the Army Medical Museum; Lieut. Col. Fred J. Fielding, chief of Classification of Records Section, Military Personnel Division; Lieut. Col. Michael E. DeBakey, chief of General Surgery Branch, Surgical Consultants Division; Lieut. Col. Oliver R. McCoy, director of Tropical Disease Control Division, Preventive Medicine Service, and Major Robert L. Kaye, Corps of Engineers, commanding officer of Cinchona Research Unit.

As director of the Army Medical Museum, the citation stated, Colonel Ash "organized the most extensive tissue pathology service ever known to the world. The photographic and art service of the museum was developed, which amassed a wealth of visual material—over 40,000 black and white photographs, over 4,000 kodachromes, and over 50,000 feet of colored movies."

Lieutenant Colonel Fielding "effected the assignment and equitable distribution of medical skills. Under his guidance the entire personnel records system was coordinated and integrated to the end that available professional abilities were utilized to the maximum degree."

Lieutenant Colonel DeBakey "conceived and initiated the monthly *Bulletin of the United States Army Medical Department*, which furnished physicians all over the world with authoritative information on advances in medicine.

In the field of malaria treatment and control Lieutenant Colonel McCoy "fostered activity in the dissemination of knowledge pertinent to tropical disease control, both in professional circles and among troops," thus maintaining their health while operating in overseas areas. His "outstanding achievements in bringing into being a means of production of quinine and related antimalarials signify a magnificent contribution to mankind."

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AWARDED DISTINGUISHED SERVICE MEDAL

Col. Tracy S. Voorhees, formerly a New York attorney and president of the Long Island College Hospital, Brooklyn, was recently awarded the Distinguished Service Medal for outstanding accomplishment while serving in the Office of the Surgeon General as director of the legal division and later as director of the control division. Colonel Voorhees is now on duty as assistant to the Secretary of War in the handling of matters affecting the medical department, with particular reference to the care of the sick and wounded and the demobilization of medical personnel.

HEALTH OF SOLDIERS IN PACIFIC AREAS REPORTED GOOD

Brig. Gen. Raymond W. Bliss, Deputy Surgeon General of the Army, in a report of his recent tour of Pacific theaters, stated that American soldiers in the Pacific are an exceptionally healthy body of troops despite the fact that many of them are located in the most disease ridden areas in the world.

The low disease rate among American forces in those areas is the result of the program of preventive medicine, involving the expenditure of millions of dollars, which the Surgeon General's Office inaugurated to guard the welfare of this country's fighting forces. To accomplish these results the Army Medical Department took the initiative in organizing an all out attack against disease. The cooperation of the best civilian and military tropical medicine experts in the country was enlisted, special courses were organized to teach army doctors how to care for troops exposed to these strange diseases, and a campaign of education in hygiene and field sanitation was inaugurated among the soldiers. Protective clothing, new repellents and insecticides, including DDT and drugs such as atabrine, penicillin and the sulfonamides, all played a part in this effective program.

The purpose of the trip was the study of medical service in the Pacific, demobilization of medical department personnel and the adoption of plans for the permanent hospitalization and evacuation of the army of occupation.

APPOINTED PLASTIC SURGERY CONSULTANT

Col. James B. Brown, chief of plastic surgery at Valley Forge General Hospital, Phoenixville, Pa., was recently appointed senior consultant in plastic surgery to the Surgeon General.

ARMY AWARDS AND COMMENDATIONS

Lieutenant Colonel Franklin C. McLean

Lieut. Col. Franklin C. McLean, now professor of pathologic physiology at the University of Chicago, who served during the war in the Chemical Warfare Service of the United States Army, was recently awarded the Legion of Merit. Dr. McLean, who was director of toxicology for the Chemical Warfare Service from October 1943 to March 1944, received the citation for his demonstration of remarkable talents and scientific versatility in laboratory and field testing and in improving the effectiveness of persistent blister and other gases. In addition to his work at Edgewood Arsenal Dr. McLean was chief of the Persistent Section of the San Jose Project in Panama. The citation was conferred also for his work as a member of the British-American coordination staff from June 1944 to September 1945, in which he was a factor in evaluating the biologic aspects of all research and testing of gas warfare equipment performed by the United States and the British commonwealth. Previous to receiving his commission as lieutenant colonel Dr. McLean was director of the toxicity laboratory of the University of Chicago and resumed his duties there as professor of pathologic physiology on Oct. 1, 1945.

Lieutenant Colonel Morton H. Flaherty

The Army Commendation Ribbon was recently awarded to Lieut. Col. Morton H. Flaherty, White Plains, N. Y., for meritorious service as assistant to the surgeon and as surgeon, Eastern Defense Command, with Headquarters at Governors Island, N. Y., from Jan. 8, 1943 to Dec. 31, 1945. "Through his experience, professional ability, keen analytical mind and conscientious effort," says the citation, "he was of very material assistance in the maintenance of adequate hospitalization and medical service for units of this command. He is to be particularly commended for his efforts in maintaining an exceptionally low rate for contagious diseases in this command in spite of rigorous climatic conditions and isolated facilities." Dr. Flaherty graduated from Columbia University College of Physicians and Surgeons, New York, in 1935 and entered the service May 15, 1941.

Major William Clinton Calvert

The Soldier's Medal was recently awarded to Major William C. Calvert, West Orange, N. J., "for heroism near Antwerp, Belgium, on Feb. 23, 1945. When a flying bomb landed in a village near his headquarters Major Calvert with three enlisted men immediately went to the scene to administer medical aid. On arriving they discovered that a child was trapped in the

wreckage of a house. Completely disregarding his own safety, Major Calvert crawled into the cellar despite the danger from an overhanging mass of cement and steadily rising water from a broken main and held the child's head above water for nearly three hours until she could be removed to safety. Major Calvert's coolness, courage and devotion to duty reflect the highest credit on himself and the Army of the United States." Dr. Calvert graduated from New York Medical College, Flower and Fifth Avenue Hospitals, New York, in 1929 and entered the service July 18, 1942.

Captain William S. M. Ling

An Oak Leaf Cluster to the Bronze Star was recently awarded to Capt. William S. M. Ling, New York, "for meritorious achievement in connection with military operations in Italy from Jan. 15 to April 9, 1944. As battalion surgeon of the 751st Tank Battalion Captain Ling displayed outstanding courage and exceptional professional ability during the preparation, the actual landing and subsequent action of the battalion at the Anzio beachhead. Owing to the special situation it was necessary for men to remain in their tanks for days at a time and without relief. This made it very difficult on crewmen, and many of the men began to complain of claustrophobia, or that the tanks seemed to be closing in on them. It was due to Captain Ling's personal attention to these men that many of them remained on duty and were not sent back to rear areas as battlefield exhaustion cases. He was untiring in his efforts and demonstrated a vast knowledge of his medical profession in fearlessly proceeding under intense fire to treat men who had been wounded and needed his care." Dr. Ling graduated from the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, in 1940 and entered the service Sept. 1, 1941.

Captain Robert Boyd Stith

The Bronze Star was recently awarded to Capt. Robert Stith of Florence, S. C., for meritorious services in support of combat operations from Nov. 9, 1942 to May 2, 1945 in North Africa and Italy. "As assistant chief of the medical division in an evacuation hospital," reads the citation, "Captain Stith rendered outstanding service of the skilled care and treatment of thousands of patients working under severe conditions of weather and enemy action. By his diligent performance he provided a constant inspiration and example to the officers, nurses and men working under him. In charge of the preoperative ward on the Anzio beachhead, Captain Stith calmly and skilfully performed his duties during periods of enemy shell fire and by his conduct influenced attainments, persevering efforts and devotion to duty. Captain Stith contributed immeasurably to the success of his unit's medical mission." Dr. Stith graduated from Duke University School of Medicine in 1935 and entered the service April 15, 1942.

Lieutenant Colonel Weldon J. Walker

Lieut. Col. Weldon J. Walker, formerly of Los Angeles, was recently awarded the Bronze Star "for meritorious service in connection with military operations against the enemy in Germany between April 3, 1945 and May 8, 1945. Lieutenant Colonel Walker, commanding officer, exerted constant and untiring effort to render superior medical service to units of the 3d Corps. Dangerous reconnaissances made personally, at a time when the front lines were in a fluid condition, enabled him to maintain liaison with these supported organizations. His initiative, diligence, sense of responsibility and considered judgment reflect credit on himself and the Army." Dr. Walker graduated from the College of Medical Evangelists, Los Angeles, in 1940 and entered the service July 12, 1941.

NAVY

BIOLOGIC WARFARE STUDIED BY THE NAVY

For two and a half years a Navy project was secretly undertaken at the University of California, Berkeley, of joint Army, Navy and civilian cooperative research in the field of biologic warfare, which was not announced until recently by the Navy Department. The group was composed of twelve officers and nine enlisted men when the project was undertaken in April 1943 under the command of Capt. Albert Paul Krueger (MC), U.S.N.R., but increased to nineteen officers and forty-five men by VJ day.

Much must still remain untold, but after thirty-three months of hazardous and painstaking study it may now be revealed that:

1. Considerable knowledge has been gained in mass defense against possible enemy employment of a certain disease which is highly fatal.

2. Laboratory and field data have been gathered which demonstrate that a man-made epidemic as an instrument of war is a likely possibility.

3. A protective suit, with self-contained oxygen supply, has been devised for the use of workers in any prospective rescue or decontamination operation.

4. Conclusive information has been obtained which would be of great value not only for protection from bacterial attack but for control of communicable airborne diseases among a peacetime population.

The disease in question, the identity of which must still be withheld, is centuries old, it is said, and one of the greatest of killers. Captain Krueger stated that the "program was undertaken not from the standpoint of academic research but with a view of obtaining short term practical results with regard to offensive possibilities and defensive countermeasures."

The precautionary measures taken during the study were so efficient that no infections due to the organisms studied occurred among the investigators. The work of this group, known as Naval Medical Research Unit No. 1, is continuing, coordinated by the Bureau of Medicine and Surgery with the Army-Navy biologic warfare program.

VICE ADMIRAL McINTIRE AWARDED DISTINGUISHED SERVICE MEDAL

The Distinguished Service Medal was recently awarded to Vice Admiral Ross T. McIntire, Chief of the Bureau of Medicine and Surgery since Dec. 1, 1938 and Surgeon General of the Navy. He was cited for his extraordinary ability in planning and applying the medical program for the Navy and Marine Corps, the citation emphasizing his "exceptionally meritorious service to the government of the United States in a duty of great responsibility as chief of the Bureau of Medicine and Surgery and Surgeon General of the Navy from Dec. 7, 1941 to Aug. 31, 1945. Displaying extraordinary foresight, unerring judgment and great administrative ability, Vice Admiral McIntire directed the planning and the practical application of the vast program which provided medical care and supply for the Navy and the Marine Corps on a scale and with a degree of success unprecedented in naval warfare. His outstanding achievement had a direct and vital part in the successful prosecution of the war." Vice Admiral McIntire has also received decorations from Belgium, Brazil, Denmark, France, French Morocco, Luxembourg, Nicaragua, Norway, Poland and Sweden.

NAVY AWARDS AND COMMENDATIONS

Commander Murray W. Ballenger

Comdr. Murray W. Ballenger, Medical Department, Naval Air Station, Pensacola, Fla., was recently awarded the Bronze Star. The award was made for his efforts following damage to his ship which resulted in a number of casualties. He worked tirelessly for many hours treating the wounded. "By his high professional skill," the citation reads, "he undoubtedly saved many lives. His outstanding conduct throughout has distinguished him among those performing duties of the same character." Dr. Ballenger graduated from the University of Kansas School of Medicine, Kansas City, in 1935 and entered the service Jan. 11, 1937.

Lieutenant Commander Howard Owen Smith

Lieut. Comdr. Howard Owen Smith, formerly of Marlin, Texas, was recently commended "for meritorious service in the line of his profession as a gastrointestinal and general surgeon aboard a United States Navy hospital ship from August 1944 to May 1945. During this period Lieutenant Commander Smith displayed unusual zeal in his devotion to duty and exhibited physical endurance and fortitude to an inspiring degree. His outstanding skill, knowledge and ability were materially responsible for the alleviation of pain and suffering and were instrumental in saving the lives of many men who otherwise would have died of shock or other disabling conditions. His conduct throughout was in keeping with the highest traditions of the United States Naval Service." Dr. Smith graduated from the University of Texas Medical Branch, Galveston, in 1922 and entered the service Nov. 26, 1942.

Captain Millard F. Hudson

A Letter of Commendation was recently presented to Capt. Millard F. Hudson, formerly of San Pedro, Calif., "for meritorious service as Atlantic Fleet Medical Officer on the staff of Commander Service Force, Atlantic Fleet, from June 1942 until November 1945." The citation accompanying the award stated that "Captain Hudson administered the medical affairs of the Atlantic Fleet and fulfilled the multitudinous responsibilities of his assignment with outstanding efficiency and skill. He directed and detailed assignments of all Hospital Corps enlisted personnel to the forces afloat and at outlying bases. By personal consultation, by visitation and by the preparation of many technical bulletins he materially contributed to the operational readiness of all fleet medical units to meet demands of battle. Captain Hudson's professional skill and outstanding performance of duty in a position of great responsibility reflect great credit on himself and the United States Naval Service." Dr. Hudson graduated from Vanderbilt University School of Medicine, Nashville, Tenn., in 1917 and entered the service Dec. 29, 1917.

Commodore Morton D. Willcutts

For his services as fleet medical officer on the staff of Commander, Fifth Fleet, Commodore Morton D. Willcutts, formerly of New York, was awarded the Legion of Merit. The citation accompanying the award stated that it was given "for exceptionally meritorious conduct in the performance of outstanding service as fleet medical officer on the staff of Commander, Fifth Fleet, from April to November 1945. During this period he participated in the amphibious operations to capture and occupy Okinawa and in the occupation of Japan. Commodore Willcutts with great diligence applied himself to the solution of medical problems incident to fleet operations, the handling of casualties and the health of personnel taking part. His sound judgment and excellent vision contributed to the success of these operations. When the fleet flagship was hit by a suicide plane with a bomb on May 12, with heavy casualties resulting, he took charge of the wounded on the main deck in the absence of the ship's medical officers, who were below at their battle stations. His promptness, presence of mind and professional skill were of great value on this occasion. His conduct was at all times in keeping with the highest traditions of the United States Naval Service." Dr. Willcutts graduated from the Indiana University School of Medicine, Indianapolis, in 1916 and entered the service Sept. 4, 1917.

MISCELLANEOUS

SELECTIVE SERVICE MEDAL

A letter addressed to THE JOURNAL *by Dr. E. D. Skeen of Gary, Ind., called attention to the fact that many members of draft boards from Gary have been called to Indianapolis to receive from the state director of Selective Service a certificate and a medal indicating their contribution but that the list published did not include the names of any physicians. A letter was addressed to Major Gen. Lewis B. Hershey, director of the Selective Service System, whose reply follows:*

Dear Doctor Fishbein:—I have received your letter dated Jan. 24, 1946, in which you quote a statement you have received from one of your subscribers in regard to the award of the Selective Service Medal to local board examining dentists and physicians.

Public Law 112, 79th Congress, approved July 2, 1945, provides that the Selective Service Medal and Certificate may be awarded to members of local boards, members of appeal boards, government appeal agents, local board examining dentists and physicians, members of medical advisory boards and reemployment committeemen who have completed more than two years of loyal and faithful service and to such others as may be selected by the director of Selective Service.

Under the procedure for the award of the medal, local board members, appeal board members and government appeal agents must be recommended by the state director of Selective Service. Other persons eligible for the award, including local board examining physicians, must be recommended by the appropriate local board and the state director.

Owing to production difficulties, it has not been possible to obtain sufficient medals, presentation boxes and certificates of merit to make the award to all eligible persons at the same time. For that reason the first awards are being made to local board members, appeal board members and government appeal agents.

In certain of the states the lists of eligible persons who are to be recommended by the local boards were not received in sufficient time to complete the printing of names on certificates. Approximately 35,000 certificates are in the process of printing at the present time. As soon as a sufficient supply of medals and certificates is received from the contractors, the awards will be made to all qualified persons.

The examining dentists and physicians who so patriotically served our local boards will not be ignored. It is merely a question of obtaining the medals and certificates for presentation. It is hoped that we will have the medals and certificates to make the awards during the latter part of February or the first of March.

LEWIS B. HERSHEY, *Director*,
Washington, D. C.

OFFICERS RELEASED FROM U. S. PUBLIC HEALTH SERVICE

A letter from Surgeon General Thomas Parran reveals that there were at the end of hostilities approximately 1,050 reserve medical officers on active duty with the United States Public Health Service. About 275 of these officers have been released to date. The releases are being made in accordance with a point system previously published in THE JOURNAL. Officers with 45 or more points are being released during the months of January and February. Surgeon General Parran states that it is expected that the critical score will be reduced on March 1 but that it is not possible at this time to state the extent of the reduction.

DISABLED PERSONS ASSOCIATION OF AMERICA

The Disabled Persons Association of America, Chicago, a nonpartisan and nonsectarian association, incorporated not for profit, recently announced an exclusive free selective placement service for disabled veterans. The Veterans Division has office and factory jobs available for disabled veterans, as well as some out of town jobs. Full cooperation with any and all veterans' organizations and other agencies will be given, and a request is made to the public to refer any disabled veterans in need of employment or counsel to Capt. A. L. Myers any day of the week between the hours of 9 a. m. and 1 p. m. at suite 1408, 39 South State Street, Chicago.

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PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Anderson, William O., Capt., Haleyville.
Bradford, Duke C., Col., 3121 12th Ave. N., Birmingham.
Britt, Walter S., Capt., 220 Cherry St., Eufaula.
Bryant, Henry C., Capt., 431 12th Terrace N., Birmingham.
Cobb, John M., Lt. Col., Tuskegee.
Darden, William H., Lt. Col., 2112 Noble St., Anniston.
Kendrick, James E. Jr., Lt. Col., 310 S. Park St., Greenville.
Martin, Carl T., Capt., Abbeville.
Mason, Robert E., Capt., 3802 Cliff Rd., Birmingham.
Monsky, David B., Major, 111 Ponce de Leon, Montgomery.
Motley, Jewett P., Capt., 2746 20th St., Ensley.
Parker, Paul H., Major, Margaret.
Peters, Jesse J., Major, Veterans Adm., Tuskegee.
Rowe, Mason C. Jr., Capt., 1203 Catalpa St., Dothan.
Samples, Leon D. Jr., 1st Lt., 425 12th Ave. N., Birmingham.
Shiffman, Hans P., Capt., DMD, SH, Napier Fld., Dothan.
Sparks, Thomas P., Capt., Box 325, Sylacauga.
Treherne, Alfred J., Lt. Col., Box 398, Atmore.

Arkansas

Binns, Byron Z., Major, Monticello.
Crocker, Elvis W., Capt., 1103 Porter St., Helena.
Crow, Marvin B., Capt., Warren.
Dew, Hogan A. Jr., Capt., Hamburg.
Fowler, Hollace D., Major, 412 Rosette, Little Rock.
Gaston, Cecil L. Jr., Major, Trinity Hosp., Little Rock.
Hundley, Louis K., Major, P. O. Box 439, Fayetteville.
Johnston, W. W., Major, Phillips City Health Unit, Helena.
Kay, Royal H., Capt., Cotton Belt Hosp., Texarkana.
Kirkham, Dunham, Major, 220 W. 20th St., Little Rock.
Lutterloh, Charles H., Lt. Col., 29 Circle Dr., Hot Springs.
McLain, Monroe D., Major, 909 Main St., Little Rock.
Maddox, Alfred H., Major, Elaine.
Moulton, Everett C. Jr., Capt., 935 Adelaide Ave., Fort Smith.
Phipps, W. E., Capt., 401 Ridgeroad, Pk. Hill, N. Little Rock.
Ritchie, Elmer J., Major, 621 W. 4th St., North Little Rock.
Savage, Hugh W., Major, 317 Beach St., Little Rock.
Thompson, Albert W., 1st Lt., Bentonville.
Williams, Jacob M., Capt., Monette.

Colorado

Alexander, Harry A., Major, 750 Cascade Ave., Boulder.
Barber, Edgar W., Lt. Col., 227 16th St., Denver.
Beck, Harold J., Major, 615 W. 22d St., Pueblo.
Benell, Otto E., Major, 1700 13th Ave., Greeley.
Benov, Harry, Capt., 1101 Colorado Blvd., Denver.
Emery, George D., Capt., 672 Cherry St., Denver.
Girod, Frank P., 1st Lt., Cortez.
Hill, Kenneth A., Lt. Col., 335 S. Vine St., Denver.
Karlick, Joseph R., Capt., 1936 Pearl, Denver.
McGraw, John P., Lt. Col., Box 308, Estes Park.
Peterson, Arthur E., Capt., 1905 19th Ave., Greeley.
Pingrey, Fergus R., Capt., 1801 Main Ave., Durango.
Pollice, John A., Major, 4344 Bryant St., Denver.
Porter, Whitney C., Major, 4310 E. 25th Ave., Denver.
Robinson, George L., Capt., Salida.
Rounds, Roy C., Major, 1427 Franklin St., Denver.
Ruzicka, Lawrence J., Capt., 1120 S. Broadway, Denver.
Sawyer, Kenneth C., Major, 1819 Gilpin St., Denver.
Shaw, Dwight B., Lt. Col., 702 N. Main, Pueblo.
Shrout, Cecil B., Col., Vet. Adm., Ft. Lyon.
Shumsky, Nathan S., Capt., 2058 Ivanhoe St., Denver.
Spillane, John H. Jr., Major, 30 E. Platte, Colorado Springs.
Whitehouse, Alfred E. Jr., Capt., 700 E. Aspen, Fruita.

District of Columbia

Beard, William H., Lt. Col., 2814 Connecticut Ave., Washington.
Beardsley, L. G., Col., 2650 Wisconsin Ave. N.W., Washington.
Daue, Edwin O. Jr., 1st Lt., 1129 Fern St. N.W., Washington.
Friedman, J. M., Lt. Col., 3539 Holmead Pl. N.W., Washington.
Gibson, Frank E. Jr., Major, 927 Eye St., N.W., Washington.
Gladsden, Eugene S., Major, 922 C St. S.E., Washington.
Greene, Joseph L., Capt., 2518 Tunlaw Rd. N.W., Washington.
Jeffrey, Millard, Capt., 2800 Woodley Rd. N.W., Washington.
Lyons, John H., Col. 1644 21st St., N.W., Washington.
Meisenbach, A. E. Jr., Capt., 927 17th St., N.W., Washington.
Randall, Robert S., Capt., 1944 3d St. N.W., Washington.
Ratcliffe, Harold E., Major, St. Elizabeth's Hosp., Washington.
Pekin, Thomas J., Lt. Col., 2650 Wisconsin Ave., Washington.
Reeves, G. W., Capt., 2916 New Mexico N.W., Washington.
Sterling, Harold, 1st Lt., 4102 14th St. N.W., Washington.
Sugar, Samuel J., Major, Gallinger Mun. Hosp., Washington.

Florida

Annis, Leonard S., Lt. Col., Bayshore Royal Hotel, Tampa.
Baker, Archie J., Capt., 4035 N. Alhambra Dr., Jacksonville.
Ball, William H., Major, 1005 Morrison Ave., Tampa.
Barks, Orville L., Capt., Groveland.
Edwards, Joshua L., Capt., 806 W. Duval St., Lake City.
Fox, Edward F., Major, 404 Ingraham Bldg., Miami.
Helms, John S. Jr., Lt. Col., 3314 Lykes Ave., Tampa.
Hyman, Jack, 1st Lt., 6110 Interbay Blvd., Tampa.
Morton, Henry G., Capt., 1074 S. Citrus Ave., Sarasota.
O'Donnell, William G., Capt., 712 SW 7th St., Miami.
Overstreet, Ralph M. Jr., Capt., Jackson Mem. Hosp, Miami.
Palmer, George S., 1st Lt., Box 547, Tallahassee.
Parker, Martle F., Capt., Lisenby Hosp., Panama City.
Parks, Lorenzo L., Lt. Col., State Bd. of Health, Jacksonville.
Parsons, Hugh E., Capt., 512 Maas Office Bldg., Tampa.
Ralston, Raymond H., Major, 523 E. McDonald St., Lakeland.
Sigman, Murray D., Capt., 36 Rhode Ave., St. Augustine.
Stebbins, Alvin L., Major, 803 N. Palafox St., Pensacola.

Georgia

Abram, Lewis E., Major, 816 S. Lee, Fitzgerald.
Alsup, William B. Jr., Capt., University Hosp., Augusta.
Anderson, William H. Jr., Capt., Grady Hosp., Atlanta.
Armstrong, William B., Capt., 4270 Harris Trail, Atlanta.
Bailey, Thomas E., Capt., 1833 Starnes St., Augusta.
Berry, Robert L., Capt., Villa Rica.
Cary, Howard R., Major, Milledgeville.
Evans, Albert L., Capt., 518 Park Dr., N.E., Atlanta.
Golsan, Willard R., Lt. Col., 8A Massee Apts., Macon.
Harper, Sage, Major, Wray.
Hilsman, Joe H. Jr., Capt., 72 11th St., NE, Atlanta.
Hoffman, Byron J., Capt., 768 Juniper St. N.E., Atlanta.
Huskey, Aubrey L., Major, 703 Med. Arts Bldg., Atlanta.
Ketchum, Clarence W., Major, Grady Hospital, Atlanta.
Little, Gwynne H., Capt., 119 King St., Dalton.
Litton, James H., Lt. Col., Court House, Milledgeville.
McMillan, Carl B., Major, 3996 N. Ivy Rd., Atlanta.
Martin, Walter D., Capt., PO Box 219, Shellman.
Muse, Jesse P., 1st Lt., 740 Seiler Ave., Savannah.
Niles, George A. Jr., Capt., Grady Hosp., Atlanta.
Pomeroy, William L., Major, 1421 St. Mary's Dr., Waycross.
Powers, Leander K., Capt., Guyton.
Rich, Maurice, Capt., 938 Oakdale Rd., Atlanta.
Rubin, Jacob, Capt., 910 E. 35th St., Savannah.
Schaffer, William B., Lt. Col., Box 366, Toccoa.
Smith, Charles R., Capt., Terrell Co. Health Dept., Dawson.
Sturm, R. T., 1st Lt., 1302 W. Peachtree, Apt. 108, Atlanta.
Tighe, Leo R., Major, Vet. Adm. Facility, Augusta.
Weinberg, James I., Lt. Col., 949 Courtney Dr., NE, Atlanta.

Maine

Branson, Sidney R., Capt., Main St., South Windham.
Clapperton, Gilbert, Major, 20 Ware St., Lewiston.
Colley, Maynard B., Major, Wilton.
Comeau, Wilfred J., Lt. Col., 48 Penobscot St., Bangor.
Cox, William V., Lt. Col., 82 Gamage Ave., Auburn.
Dougherty, John F., Capt., 60 North St., Bath.
Eastman, Charles W., Major, 15 Millet St., Livermore Falls.
Feeley, John R., Capt., 3 3d St., Bangor.
Finks, Henry, Major, 286 State St., Portland.
Laney, Richard P., Major, Prospect St., Skowhegan.
Lenfest, Stanley R., Capt., Waldoboro.
Lombard, Reginald T., Lt. Col., 793 Main St., South Portland.
McManamy, Eugene P., Capt., Cottage Lane, Cape Cottage.
Metzgar, John G., Capt., 31 Grove St., Augusta.
Moore, Roland B., Col., RFD 3, Portland.
Morrison, Alvin A., Major, 165 Glenwood Ave., Portland.
Moulton, Albert W. Jr., Capt., 180 State St., Portland.
Richards, Carl E., Major, Box 81, Alfred.
Webber, Wedgwood P., Major, 376 Main St., Lewiston.

Mississippi

Cohen, Emanuel, Capt., Pace.
Holley, Robert L. Jr., Capt., U. of Miss. Hosp., University.
House, Nathaniel C., Major, Belzoni.
Hudgens, John C., Lt. Col., Vet. Adm. Facility, Gulfport.
Minter, David R., Lt. Col., Rochdale.
Sims, Murphy M., Capt., Health Unit, Oxford.
Sneed, Ralph, Major, Charity Hosp., Jackson.
Wiener, William B., Capt., Canton.
Wright, Frederick L., Lt. Col., Gulfport.

PHYSICIANS SEPARATED FROM SERVICE

Nebraska

Glenn, William V., Capt., 2007 Crook St., Falls City.
Greenslit, Frank S., Capt., 1690 Sioux St., Lincoln.
Haentzschel, Lester E., Lt. Col., 2401 Ryons St., Lincoln.
Himalstein, Milton R., Capt., 1523 1st Ave., Scottsbluff.
Holden, Walter J., Capt., Elkhorn.
Horwich, Joe M., Major, 1403 N. 33d St., Omaha.
Korth, Zeno N., Lt. Col., 3426 Webster, Omaha.
Kunkel, Lloyd N., Major, Weeping Water.
Lierman, Clifford E., Capt., 112 N. 38th Ave., Omaha.
Marx, Paul D., Lt. Col., 2543 B St., Lincoln.
Miller, Samuel D., 1st Lt., 5515 S. St., Lincoln.
Millett, Clinton C., Lt. Col., 5607 Leavenworth, Omaha.
Milligan, John O., Capt., 1818 S. 24th St., Lincoln.
Nye, Dan A., Capt., 1035 J St., Lincoln.
Rose, Forrest I., Capt., 4904 Davenport St., Omaha.
Strough, LaVern C., Capt., 1123 Ella St., Beatrice.
Waddell, William W., Major, 1701 S. 4th St., Beatrice.
Wolf, William K., Lt. Col., Hay Springs.

Nevada

Bagley, Richard O., 1st. Lt., 2025 I St., Sparks.
Dolezal, Joseph B., Capt., Battle Mountain.
Felder, Lin S., Capt., Winnemucca.

New Mexico

Beam, Mark P., Major, 1608 Park Ave., Albuquerque.
Bielinski, Henry E., Capt., P. O. Box 162, East Vaughn.
Hinkle, Warren I., Major, Vet. Adm. Facility, Albuquerque.
Hodde, Henry W., Capt., 303 E. Taylor, Hobbs.
Kaufman, B. H., Capt., 1077 Indian School Rd., Albuquerque.
Kempers, Bert, Major, 530, Lafayette Pl., Albuquerque.
Merriam, Sidney A., Major, RFD 4, Box 552, Albuquerque.
Rosenbaum, Myron G., Capt., 437 N. Maple St., Albuquerque.
Setzler, Robert K., 1st Lt., Shiprock.
Tritt, Earl F., Col., Jicarilla Apache Indian Reservation, Dulce.

North Carolina

Baum, Ralph E., Capt., Kitty Hawk.
Beyer, Emil C., Major, Box 3127, Duke Hospital, Durham.
Brown, William M. B., Major, 627 Dickinson Ave., Greenville.
Cannon, Eugene B., Major, Asheboro.
Carter, Paul C., Lt. Col., Madison.
Dryden, James S., Major, Professional Bldg., Raleigh.
Harrell, Leon J., Major, RFD 3, Goldsboro.
Jones, Clyde T., Capt., West Jefferson.
Lancaster, Newton F., Major, Box 830 Waynesville.
Long, Thomas S., 1st Lt., 338 W. Main St., Washington.
McCracken, Joseph P., Major, 907 Mangum St., Durham.
Mauzy, Charles H., Capt., 824 Nissen Bldg., Winston-Salem.
Merritt, Jesse F., Major, 1615 S. College Park Dr., Greensboro.
Munroe, Colin A., Capt., 515 Oakland Ave., Charlotte.
Patterson, Hubert C., 1st Lt., 220 North St., Albemarle.
Robertson, John N., Major, 807 Hay St., Fayetteville.
Rudd, James C., Major, 249 N. Edgeworth, Greensboro.
Salter, Theodore, 1st Lt., Stacy.
Smerznak, John J., Capt., 279 Vance St., Concord.
Smith, Robert E., Capt., Mount Airy.
Woodhall, Barnes, Lt. Col., Cole Mill Rd., Durham City.

Oklahoma

Choice, Robert W., Capt., Wakita.
Foerster, H. A., Lt. Col., 806 NW 25th St., Oklahoma City.
Fox, Raymond H., Lt. Col., 915 N. Main St., Altus.
Greenberger, Edward D., Capt., 216 E. Choctaw, McAlester.
Harrison, S. P., Capt., 1701 NW 31st St., Oklahoma City.
Hendren, Walter S. Jr., Capt., 501 N.W. 12th, Oklahoma City.
Henry, Millard L., Capt., Heavener.
Hubbard, John R., Lt. Col., 1628 N.E. 11th, Oklahoma City.
Hubbard, William E., Capt., 1500 N.E. Park Pl., Oklahoma City.
Lively, Claude E., Major, 1275 S. 6th St., McAlester.
Maril, Joseph J., Major, 816 Bell Ave., Lawton.
Neilson, William P., Lt. Col., 3200 Lahoma Rd., Enid.
Petty, James S., Major, 521 E. Logan, Guthrie.
Prosser, Moorman P., Major, Cent. Okla. State Hosp., Norman.
Records, John W., Major, 2523 N. Dewey, Oklahoma City.
Reiff, William H., Capt., 500 N.E. 15th, Oklahoma City.
Rutherford, Vester M., Major, Box 75, Woodward.
Scott, George W., Capt., Tishomingo.
Shofstall, William H., Capt., 1445 N. Main St., Tulsa.
Smith, Carlton E., Major, 123 N. 4th St., Henryetta.
Stout, Hugh A., Capt., 809 N. Beard St., Shawnee.
Watson, Isaac N., Lt. Col., 439 E. Ayers, Edmond.
Weaver, William N., Lt. Col., 408 S. 12th St., Muskogee.
Wheeler, Homer C., Capt., Sallisaw.

Oregon

Mac Dougall, Walter H., Capt., Box 304, Lakewood, Oswego.
Morris, David A., Capt., 1225 Mill St., Eugene.
O'Donnell, Richard H., Capt., 3537 S.E. Main, Portland.
Ray, George L., Capt., 808 NE 23 Ave., Portland.
Reed, Robert J., Capt., 3816 N.E. 33d Ave., Portland.
Strohm, John G., Col., 610 S.W. Alder St., Portland.
Warnell, Charles E., Capt., 6109 SE Belmont, Portland.

Rhode Island

Barry, Ambrose G., Capt., 20 Prince St., Pawtucket.
Dunstan, Paul L., Capt., State Hosp. Mental Dis., Howard.
Horvitz, Abraham, Capt., 127 Gallatin St., Providence.
McDonnell, William A., Capt., 88 Jefferson St., Providence.
McIntyre, William A., Capt., 132 Whitford Ave., Providence.
Melvin, Edward G., Major, 57 Albert Ave., Cranston.
Nestor, Thomas A., Major, 710 N. Main St., Providence.
Perry, Thomas Jr., Capt., 46 Pitman St., Providence.
Rogell, Harold I., Lt. Col., 377 Angell St., Providence.

Virginia

Alexander, John E., Major, Vienna Medical Center, Vienna.
Buckley, Michael L., Major, 2507 N. Pershing Dr., Arlington.
Cantor, Hyman, Capt., 17 Wythe St., Petersburg.
Driscoll, William D. R., 1st Lt., 518 Riverside Ave., Covington.
Edwards, Hugh R., Lt. Col., Buxton Hosp., Newport News.
Humphries, Thomas J., Capt., 1141 2d St. S.W., Roanoke.
Jones, Herbert C., Lt. Col., 1638 Westover Ave., Petersburg.
Jones, William R. Jr., Capt., 1004 West Ave., Richmond.
Judson, John H., Capt., 6121 N. 18th St., Arlington.
Kirchner, John A., Capt., Hercules Powder Co., Radford.
Larkum, Newton W., Lt. Col., Box 1384, Charlottesville.
Nalls, Walter L., Lt. Col., 3110 Grove Ave., Richmond.
Phipps, Glenn W., Capt., PO Box 74, Independence.
Pritchett, Drake, Capt., 108 W. Main St., Danville.
Robertson, Rowland H. Jr., Capt., Lewis-Gale Hosp., Roanoke.
Robins, Charles R. Jr., Major, Stuart Circle Hosp., Richmond.
Rowe, Carter R., Major, 1200 Prince Edward, Fredericksburg.
Siersema, Reynold C., Major, 120 Westmoreland, Richmond.
Snider, John D., Capt., Ashburn.
Sproul, Alexander E., Capt., E. Beverly St., Staunton.
Stanley, Robert R., Capt., Charlottesville.
Steinberg, Harry, Major, Box 64, Bastian.
Verdel, Louis F., Col., Vet. Adm., Roanoke.
Wolfe, Frank B., 1st Lt., Coeburn.

Washington

Black, John J., Major, 209 E. 9th, Ellensburg.
Carter, Ronald P., Major, 3216 W. 58th St., Seattle.
Gunderson, Harold J., Capt., 1011 Grand, Everett.
Judd, Herman S. Jr., 1st Lt., West. State Hosp., Ft. Steilacoom.
Kroger, Orville C., Capt., 114 W. Magnolia, Centralia.
Lyons, Clinton G., Major, 6061 7th Ave. N.E., Seattle.
Meyer, William V., Capt., 1006 Colby Ave., Everett.
Nakashima, Victor K., Capt., 1017 Jackson St., Seattle.
Overley, Harold G., Capt., % C. J. Alexander, Prosser.
Petrone, Rosco E., Capt., American Lake.
Proffitt, Josiah C., Lt. Col., 4710 University Ave., Seattle.
Wham, Manley J., Capt., Holden.

Wisconsin

Behnke, C. H., Capt., 8410 Watertown Plank Rd., Wauwatosa.
Bitter, Reuben H., Major, 85 Oakland Ave., Oshkosh.
Dorn, Anton S., Capt., 1535b N. 15th St., Milwaukee.
Dunker, George O., Capt., 2302 E. Beverly Rd., Milwaukee.
Finn, Walton C., Major, 20 Forest Ave., Fond du Lac.
Gosman, Joseph A., Capt., 423 Main St., Racine.
Hartman, Ralph F., 1st Lt., 802 Court St., Janesville.
Heil, Julius V., Capt., 1445 W. Forrest Home Ave., Milwaukee.
Joachim, Frederick G., Major, 1619 Monroe St., Madison.
Kalb, Clifford H., Capt., Grafton.
Lewis, Russell F. Jr., Capt., 202 E Ave. S., Waukesha.
Liberman, David L., Major, Vet. Adm. Facility, Wood.
McRoberts, Jerry W., Lt. Col., 1735 N. 7th St., Sheboygan.
Mallow, Harvey G., Capt., 312 Main St., Watertown.
Meyer, Kilian H., Capt., 2130 E. Locust St., Milwaukee.
Mokrohisky, Stephen M., Major, 912 E. Mason St., Green Bay.
Reinardy, Everett W., Major, 633 Washington St., Burlington.
Sagi, Joseph H., Capt., 1609 N. Prospect Ave., Milwaukee.
Salinsky, Lester V., Major, 1923 N. 13th St., Sheboygan.
Tripodi, Donald W., Major, 3205 W. Wisconsin, Milwaukee.
Weston, Frank L., Col., 166 Lakewood Blvd., Madison.

Canal Zone

Goerger, Verne F., 1st Lt., Gorgas Hosp., Ancon.
Hooper, Rector C., Capt., Gorgas Hosp., Ancon.

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MEDICAL OFFICERS RELEASED BY THE NAVY

NAVAL RESERVE MEDICAL OFFICERS RECOMMENDED FOR RELEASE FROM ACTIVE DUTY

Alabama

Holmes, William C.....Foley
Peters, George S.....Montgomery

Arizona

Rice, Philip E.....Glendale

Arkansas

Amis, James W.....Fort Smith
McLochlin, Ralph E.....Little Rock

California

Anderson, Herbert, Jr.....Los Angeles
Arkush, Albert S.....Brentwood Heights
Arthur, James M.....Fresno
Bennett, Dudley W.....San Francisco
Brown, Harrison B.....San Francisco
Campbell, James V.....Oakland
Carter, Marshall L.....Los Altos
Chew, William B.....Berkeley
Clark, Frank B.....Long Beach
Feingold, Benjamin F.....Los Angeles
Fisher, Robbin E.....Pomona
Folsom, Clarence H.....San Marino
Fraser, Harold E.....San Francisco
Frug, James B.....Berkeley
Gaw, Emir A.....San Diego
Goldman, Alfred.....San Francisco
Graeser, James B.....Oakland
Graves, Charles A.....Beverly Hills
Haigh, John S.....Pasadena
Haley, Philip S.....San Jose
Harrall, Pinckney.....San Francisco
Harrington, John T.....San Francisco
Hartsough, Christopher W., Jr..San Diego
Hill, Harold A.....San Francisco
Hockenbeamer, Ernest P.....San Jose
Hull, Eugene H.....San Bernardino
Hunter, James T.....Los Angeles
Johnson, Robert W.....San Francisco
Josephson, Joseph B.....San Jose
Kelley, Harry W.....Oakland
Lapin, Morey.....Los Angeles
MacPherson, Fraser L.....San Diego
Manley, Donald J.....Hayward
Martin, Hugh H.....Riverside
McMaster, Paul E.....Beverly Hills
Meamber, Donald L.....Montague
Mensor, Merrill C.....San Mateo
Michael, Paul .....Piedmont
Moore, James W.....Ventura
Myers, Orris R.....Eurecka
Nesting, Orlando S.....Vallejo
O'Hara, Francis P.....San Diego
O'Meara, Francis P.....Bakersfield
Parker, Thomas.....Laguna Beach
Pederson, Allen J.....Santa Cruz
Pfaff, Richard O.....San Jose
Purcell, Howard M.....Los Angeles
Redell, John C.....San Diego
Regan, James F.....Los Angeles
Roen, Paul B.....Los Angeles
Roller, Charles S.....Woodland
Salvadorini, Vasco A.....Hayward
Schneider, Elliot G.....San Francisco
Shelby, Donald C.....Los Angeles
Smith, Daniel D.....Watsonville
Smith, Frank H.....Salinas
Smith, Joseph G.....Berkeley
Spessard, Thomas N.....Oakland
Stephens, Bruce Miller.....Piedmont
Sumner, Wendell W.....Escondido
Surridge, Robert C., Jr.....Los Angeles
Tattersall, Kenneth L.....Oakland
Vaughn, John O.....Santa Monica
Vieira, Frank G.....Stockton
Vincent, Robert P.....Corona Del Mar
Wentz, Arthur E.....Santa Barbara
Wharton, Charles W.....Los Angeles
Wilson, Llewellyn E.....Anaheim
Zumwalt, Reuben H.....San Francisco

Colorado

Marsh, John W.....Greeley
Miles, Martin B.....Boulder
Shull, Clarence W.....Glenwood Springs

Connecticut

Campbell, Sherburne.....Meriden
Curley, William H., Jr.....Bridgeport
Friedman, Nathan H.....Bridgeport
Neff, William E., Jr.....Cheshire
O'Meara, Francis P.....Darien
Quimby, Robert L.....West Hartford
Sponzo, James J.....Hartford
Strongin, Herman F.....Groton

Delaware

Bowdle, Frederick A.....Wilmington

District of Columbia

Greenberg, Milton M.....Washington
McCarthy, Charles L.....Washington
Monat, Henry A.....Washington
Moss, Leland C.....Washington

Florida

Anderson, Thomas M.....Eustis
Bowser, Frank E.....Key West
Eichert, Herbert .....Miami
King, Raymond H.....Jacksonville
Maxwell, Eugene B.....Miami Beach
McClamroch, James M.....Gainesville
Payton, Frazier J.....Miami Beach
Phillips, Kenneth.....Miami
Richardson, John R.....Miami Beach
Sory, Bailey B., Jr.....Palm Beach
Tribble, Charles E.....DeLand
Turk, John P., Jr.....Miami
Wattles, Frank M.....Jacksonville

Georgia

Ansley, Robert B.....Decatur
Fort, Lynn, Jr.....Atlanta
Hailey, Hugh E.....Atlanta
Mitchell, Marvin A.....Atlanta
Ridley, John H.....Atlanta
Roberts, Charles P.....Atlanta
Rogers, John H.....Atlanta
Wilson, Richard B.....Atlanta
Wright, Edward S.....Atlanta

Illinois

Baird, Blanchard M.....Marissa
Barry, Fravel S.....Glenview
Benjamin, Eustace I.....Evanston
Blender, William, Jr.....Peoria
Ford, William K.....Rockford
Gladish, Donald G.....Glenview
Greene, Ronald R.....Chicago
Greer, Miller .....Vandalia
Harris, John J.....Chicago
Lebensohn, James E.....Chicago
Martin, George A.....Chicago
Mennella, James V.....Chicago
Meyer, Joseph C.....Chicago
Moore, Lawrence M.....Benton
Rainey, Clarence W.....Wilmette
Rambar, Alwin C.....Chicago
Roberts, Dewey M.....Alton
Sankstone, Manning I.....Chicago
Shambaugh, Philip .....Chicago
Sours, James W.....Peoria
Stephens, Harry H.....Oak Park
Stevens, John W.....Du Quoin
Wyman, George J.....Dixon
Zimmerman, Edward F.....Chicago

Indiana

Ash, Herold H.....Lafayette
Fleming, Justus M.....Elkhart
Gehres, Robert W.....Shelbyville
Long, Max R.....Marion
Tharp, Ray .....Indianapolis

Iowa

Abbott, Walter D.....Des Moines
Buresh, Abner.....Lime Springs
Collins, Robert M.....Council Bluffs
Fritchen, Arthur F.....Decorah
Gallagher, John P.....Oelwein
Graeber, Frederick O.....Des Moines
Hughes, Robert O.....Ottumwa
Krauel, Louis H.....Cedar Rapids

Kansas

Algie, William H.....Kansas City
Anderson, Donald A.....Salina
Wood, Lawrence E.....Kansas City

Kentucky

Bell, George M.....Ashland
Glenn, John P.....Russellville
Parks, Stanley S.....Lexington

Louisiana

Bristow, Louis J., Jr.....New Orleans
Danna, Pascal L.....New Orleans
Hattaway, Milton M.....New Orleans
Little, Archibald A.....New Orleans

Maine

Hurd, Allan C.....Gardiner
Mandelstam, Abe W.....Lewiston

Maryland

Flynn, Philip D.....Baltimore
Holden, Frederick A.....Baltimore
Karfgin, Arthur .....Baltimore
Thomas, Bernard O., Jr.....Frederick
Wheeler, Howard L.....Baltimore

Massachusetts

Alt, Richard E.....Beverly
Bennett, Henry S.....Brookline
Byrnes, James E.....Holyoke
Carmody, John T. B.....Paxton
Chute, James L.....Osterville
Dolan, Ralph F.....Boston
Dupre, Frederic E.....Worcester
Feldman, Noah N.....Holyoke
Hayes, John J.....Boston
Hoyt, Lyman H.....Brookline
Johnson, Carroll W.....Worcester
Macaluso, Anthony.....W. Newton
McHugh, Edward J.....Holyoke
McLean, Sterling A.....Middleboro
Palmer, Robert S.....Brookline
Ritchie, Morris J.....Westfield
Schmidhofer, Ernst.....Boston
Smith, Edward C.....Brookline
Sprague, Howard B.....Chestnut Hill
Tudor, Frederic .....Milton
Weiner, Fred F.....Brockton
Wills, Arthur A.....Braintree
Zupanec, Ralph .....Boston

Michigan

Abbott, Vernon C.....Pontiac
Aldrich, Leonard C.....Houghton
Ambrose, Jesse C.....Melvindale
Anderson, Gordon H.....Dearborn
Belanger, Ernest E.....River Rouge
Bonifer, Philip P.....Battle Creek
Conover, George Van A.....Flint
Driscoll, John J.....Detroit
Grigg, Arthur P.....Saginaw
Gugino, Frank J.....Reese
Hill, Harold C.....Howell
Jones, Horace C.....Detroit
Klaus, Cyril D.....Grand Rapids
Miller, Hugh A., Jr.....Detroit
Salot, Russell F.....Mt. Clemens
Slack, Walter K.....Saginaw
Sowers, Bouton F.....Benton Harbor
Strom, Arthur W.....Hillsdale
Teed, Reed W.....Ann Arbor
Young, Donald C.....Detroit

MEDICAL OFFICERS RELEASED BY THE NAVY

Minnesota

Funk, Victor E. ..... Oak Terrace
Lannin, Donald R. ..... Mabel
Neel, Harry B. ..... Albert Lea
Rice, Hagbart G. ..... Thief River Falls
Sorem, Milton B. ..... St. Paul
Travis, James S. ..... St. Paul
Van Bergen, Frederick H. ..... Minneapolis
Weis, Benjamin A. ..... St. Paul
Westrup, John E. ..... Lanesboro

Mississippi

Donaldson, Frank A. ..... Oakland
Lipscomb, Lee Mc. ..... Jackson

Missouri

Atwell, Floyd C. ..... St. Louis
Bartlett, Willard, Jr. ..... St. Louis
Bassett, Sam A. ..... St. Louis
Carney, Joseph E. ..... St. Louis
Coburn, Donald F. ..... Kansas City
Flanders, Horace F. ..... Kansas City
Hartnett, Leo J. ..... St. Louis
Hurst, Ben B., Jr. ..... Rock Port
Hurst, Wilfred W. ..... Joplin
Johnstone, Paul N. ..... Kansas City
Kinman, Lindell M. ..... Normandy
Klein, Edward H. ..... Kansas City
Mooney, Marcel L. ..... Kansas City
Mordaunt, Richard H. ..... St. Joseph
Schuhmacher, Nelson R. ..... Liberty
Skinner, John S. ..... Clayton

Nebraska

Abts, Eugene J. ..... Randolph
Ferciot, Charles F. ..... Lincoln
Francis, Norton L. ..... Bancroft
Kappus, Harold C. ..... Omaha
Kilgore, Robert N. ..... York
Morgan, Donal H. ..... McCook
Waltemath, Glen F. ..... North Platte

New Hampshire

Lee, Theodore H. ..... Troy
Walker, Thomas B. ..... Portsmouth

New Jersey

Byer, Maurice Y. ..... Trenton
Davidoff, Manuel A. ..... Newark
Dorris, Earl D. ..... Cedar Grove
Dunham, Malcolm M. ..... Woodridge
Eccleston, Herbert H. ..... Hackensack
Finnerty, Urban R. ..... Montclair
Gerner, Harry E. ..... Jersey City
Goldstein, Robert ..... Dover
Hummel, Ira L. C. ..... Salem
Ill, Herbert M. ..... Glen Ridge
Morton, David P. M. ..... E. Orange
Mustermann, Otto H. ..... Union City
Parsonnet, Eugene V. ..... Newark
Rainey, Willard G. ..... Princeton
Romano, Vincent E. ..... Newark
Schlossbach, Theodore ..... Ocean Grove
Seybold, Arthur D. ..... Plainfield
Tirrell, Chester M. ..... Newark
Tomec, Richard F. ..... Montclair
Yaguda, Asher ..... Newark

New Mexico

Pate, Henry D. ..... Carlsbad

New York

Berkowitz, Abraham ..... New York
Berman, Harold H. ..... Ogdensburg
Bernstein, Phineas ..... New York
Bookman, Ralph ..... New York
Buscemi, Arthur A. ..... Jackson Hts., L. I.
Childs, Edward P. ..... New York
Daley, William J. ..... Buffalo
Dargeon, Harold W. K. ..... New York
Delbridge, Ralph E. ..... Rochester
Dell'Aquila, Dominic J. ..... New Rochelle
De Santo, Dominic A. ..... New York
Ehrlich, Harry ..... Brooklyn
Feld, Harold ..... Brooklyn

New York—Continued

Fitch, Leston E. ..... New York
Fournier, Louis G. ..... Syracuse
Gallaher, Charles S. ..... Rochester
Gilbert, George A. ..... Schenectady
Gilbert, Joseph G. ..... Brooklyn
Goldwater, Leonard J. ..... New York
Graham, Allan S. ..... Mt. Vernon
Granet, Emil ..... New York
Greene, Oscar ..... New York
Hammill, Hamilton J. ..... Pelham
Harrison, Alvie B. ..... New York
Hauser, Louis A. ..... New York
Heckel, George P. ..... Rochester
Holzsager, Theodore G. ..... Brooklyn
Horton, Arthur J. ..... St. Albans
Jaleski, Thomas C. ..... Larchmont
Kelly, LeMoyne C. ..... Rochester
Kruger, Alexander W. ..... New York
Lane, Joseph A. ..... Rochester
Lange, Henry P. ..... Brooklyn
Leider, Morris ..... Brooklyn
Livingston, Edward M. ..... New York
MacDonald, William J. ..... Buffalo
Marting, Frank L. ..... Schenectady
McCarthy, William J. ..... Brooklyn
McCormick, Geo. W. ..... Staten Island, L. I.
Medd, Charles L. ..... Manhasset
Meek, Raymond E. ..... New York
O'Neill, Francis J. ..... Binghamton
Paladino, John L. ..... Brooklyn
Paterno, Joseph G. ..... Brooklyn
Potter, Leman W. ..... White Plains
Scharbius, Alfred A., Jr. ..... Long Island
Schneller, Arthur ..... Long Island
Schrade, Alfred M. ..... Bronx
Strully, George J. ..... Bronx
Trivilino, Alfred A. ..... Jamaica, L. I.
Vogel, Henry E. ..... Buffalo
Wald, Oscar ..... Brooklyn
Woodworth, Everett A. ..... Kenmore

North Carolina

McDonald, Angus M. ..... Charlotte

Ohio

Bachman, Robert V. ..... Cleveland
Beal, Lynn E. ..... Toledo
Cheek, Paul E. ..... Columbus
Crile, George, Jr. ..... Cleveland Heights
Davies, Drew L. ..... Columbus
Domall, Edwin E. ..... Toledo
Forrester, Charles R. ..... Toledo
Fronek, Otis J. ..... Cleveland Heights
Gardner, George E. ..... Lancaster
Gaspari, Emidio L. ..... Toledo
Gillette, Robert S. ..... Toledo
Gold, Michael J. ..... Dayton
Masters, William E. ..... Columbus
Michael, Oscar J. ..... Danville
Myers, Stanley A. ..... Youngstown
Obenour, Sterling W. ..... Zanesville
Seyler, Lloyd E. ..... Dayton
Thomas, Berger ..... Columbus

Oklahoma

Blue, Johnny A. ..... Guymon
Devanney, Phil J. ..... Sayre

Oregon

Boyer, John M. ..... Portland
Campbell, James E. ..... Roseburg
Enkelis, Jacob J. ..... Portland
Johnsrud, Russell L. ..... Portland
Sharkey, William P. ..... Portland
White, Leslie A. ..... Eugene

Pennsylvania

Androsky, Bernard S. ..... Pittston
Bortz, Edward L. ..... Philadelphia
Brant, Robert E. ..... Phoenixville
Brown, Clark E. ..... Philadelphia
Clutz, Paul A. ..... Mercersburg
Conoway, Horace B. ..... Philadelphia

Pennsylvania—Continued

Conrad, Chester A. ..... Palmyra
Conrad, Roy G. ..... Lebanon
Farmer, Rodney A. ..... Greensburg
Freeman, Eliot N., Jr. ..... Schuylkill Haven
Hartman, William F. ..... Lancaster
Kintzing, William B. ..... Hanover
McNair, Stirling S. ..... Wayne
Moyer, Raymond C. ..... Philadelphia
Peters, James M. ..... Philadelphia
Rech, Joseph F. ..... Reynoldsville
Richardson, Clesson W. ..... Philadelphia
Silcox, Louis E. ..... Philadelphia
Someborn, Robert M. ..... Pittsburgh
Wycoff, William C. ..... Pittsburgh

Rhode Island

Bray, Russell S. ..... Providence
Londergan, James P. ..... Providence
Marks, Herman B. ..... Pawtucket
O'Brien, Thomas J. ..... Newport
Stephens, Henry F. ..... Barrington

South Carolina

McInnes, George F. ..... Charleston

Tennessee

Anderson, Joseph D. ..... Franklin
Gresham, Charles S. ..... Johnson City
King, John C. ..... Memphis
Zimmerman, Dan J. ..... Morristown

Texas

Aten, Eugene L. ..... Dallas
Buehler, Martin S. ..... Dallas
Bush, Leonard E. ..... Huntsville
Cairns, Arthur B. ..... Dallas
Cox, Lyman T. ..... El Paso
Curb, Delos G. ..... Albany
Duggan, Le Roy B. ..... Houston
Duncan, Horace E. ..... Dallas
Fox, Everett C. ..... Dallas
Grow, Max H. ..... Dallas
Hamill, Dan B. ..... Corsicana
Heath, Jesse B. ..... Madisonville
Kelley, Richard E. ..... Houston
Kerbow, Dock F. ..... Paris
Kildee, Henry A. ..... Portland
Koontz, Lee A. ..... San Antonio
Margraves, Ross D. ..... Houston
McKenzie, Walten H. ..... Ft. Worth
Peek, John S. ..... Brownsville
Rhine, Leland R. ..... Tyler
Robert, William P. ..... Beaumont
Roberts, Joseph D., Jr. ..... Longview
Spence, Harry M. ..... Dallas
Young, Jack G. ..... Dallas

Vermont

Coyle, John A. ..... Norwich

Virginia

Bondurant, Charles H. ..... Roanoke
Fugate, Robert C. ..... Roanoke
Gemmill, Thomas L. ..... Radford
Johns, William A. ..... Richmond
Marable, James E. ..... Newport News
McGuire, William P. ..... Winchester
Schafer, William L., Jr. ..... Alexandria

Washington

Collins, William W. ..... Sunnyside
Galbraith, James E. ..... Seattle
Joers, Lawrence E. C. ..... Tacoma
Le Cocz, Edward A. ..... Seattle

West Virginia

Bird, James D., Jr. ..... Elm Grove, Wheeling
Dobbs, Lee F., Jr. ..... Wheeling
French, August M. ..... Logan
Smith, Clyde A. ..... Beckley

Alaska

Walkowski, August S. ..... Anchorage

ORGANIZATION SECTION

Washington Letter

(From Our Regular Correspondent)

Feb. 4, 1946.

Opinions of Blue Cross President on National Health Problem

John R. Mannix, national chairman of the Blue Cross Plans for hospitalization, told members of the Blue Cross commission at the quarterly meeting that federal legislation would not be necessary to solve the national health problem. He based this opinion on a current membership of 20 million persons and a weekly enrolment of 100,000 in the organization. The nonprofit group has a membership of 3,500 hospitals. The commission set up a special group to study provision of additional hospital facilities for veterans. Mr. Mannix said that a national health program should permit enrolment of self-employed persons in a hospital plan. Members of the commission besides Mr. Mannix are M. Haskins Coleman, Richmond, Va., vice chairman; George Putnam, Boston, treasurer; Dr. Louis E. Jarrett, New Orleans; Ray F. McCarthy, St. Louis; Dr. Basil C. MacLean, Rochester, N. Y.; E. A. van Steenwyk, Philadelphia; Msgr. R. Marcellus Wagner, Cincinnati; F. A. Wardenburg, Wilmington, and C. Rufus Rorem, Chicago, director of the national organization.

Nurses' Memorial Campaign Gets Off to Good Start

The campaign to raise $2,000,000 to erect a nurses' national memorial in Washington has been launched with considerable success. At a Washington meeting, at which Mrs. Harry S. Truman was guest of honor, $150,000 in initial pledges was obtained. The memorial will take the form of a social center or home for nurses and other women in the armed forces medical corps. Surg. Gen. Norman T. Kirk, principal speaker, paid tribute to the work done by the 57,000 army nurses who served during the war. He mentioned the nurses on the Anzio beachhead who performed their duties within range of enemy fire. He also lauded Capt. Gladys Mealer, chief nurse in the tunnel at Corregidor, and the 55 nurses, the dietitian and the physical therapist who "sweated in the hell of the Santo Tomas internment camp for almost three years with nothing but rice to eat for most of the time and not enough of that." "The real monument to the work of the army nurse is enshrined in the hearts of the men they served so well," he said.

Development of "Cosmetic" Artificial Hand at Walter Reed

Although cautioning against overoptimism, Lieut. Col. Donald B. Slocum, director of the Walter Reed Hospital laboratory, reports that a new type of "cosmetic" hand, which "looks like one and can be used like one," has been developed at the hospital. Progress is reported in the efforts of Major Charles A. Jackson, dental officer, and T/3 C. O. Anderson and others who are utilizing plastics of which dentures are made to develop lifelike hands that can be worn without gloves. A staff of eleven research engineers and highly trained technicians are working on the new "hand" in the Walter Reed laboratory. All seven of the nation's army hospitals caring for amputees are doing laboratory work, each specializing on a particular limb. Walter Bura, head of the division of prosthetic services of the Veterans Administration, states that the program will be permanent.

Antivivisection Bill to Get Hearing Next Month

A public hearing, possibly in February, has been promised on the Lemke antivivisection bill by the House District committee. Spokesmen have assured Representative Lemke, Republican of North Dakota, that his bill will have an early hearing.

Medical Legislation

MEDICAL BILLS IN CONGRESS

Scientific Research

Senator Willis, Indiana, for himself and Senator Hart, Connecticut, Senator Hawkes, New Jersey, Senator Hickenlooper, Iowa, Senator Smith, New Jersey, Senator Stanfill, Kentucky, Senator Wiley, Wisconsin, and Senator Young, North Dakota, has introduced S. 1777 to establish a National Science Foundation as a corporation, the initial members of which will be fifty recognized leaders in the fields of fundamental science, social sciences, medicine, engineering and education, and lay persons of recognized standing in public affairs. The initial members will be appointed by the President from nominations requested by him from the National Academy of Sciences for those fields within the province of the academy and from recognized national organizations in those fields outside that province. The foundation will be authorized to fill vacancies in its membership and to appoint a chief executive officer. It will be authorized to report annually to Congress on the monetary needs of American institutions with regard to research and training in all departments of science. It will aid by means of scholarships and fellowships in these departments. It will be required to request advice from the National Academy of Sciences in matters relating to the physical and biologic sciences and mathematics, including basic medicine and engineering.

Congressman Luce, Connecticut, has introduced H. R. 5332 to establish an executive department in the government to be known as the Department of Science and Research, to foster, promote and develop the study and spread of scientific knowledge and its practical application. There will be five bureaus in this department: (1) a bureau of Physics and Mathematical Science, (2) a Bureau of Public Health and Social Science, (3) a Bureau of Scientific Education and Information, (4) a Bureau of the Biological Sciences and (5) a Bureau of Engineering and Technological Sciences.

Charitable Deduction from Income Taxes

Representative Luce, Connecticut, has introduced H. R. 5296, providing that, beginning with the taxable year 1946, physicians, surgeons and dentists shall be permitted an additional credit as a deduction on their income tax equal in terms of percentages to that portion of their time each year which is devoted to charity, free clinic work and public research work.

Health of School Children

A joint resolution, S. J. Res. 137, has been introduced by Senator Morse, Oregon, proposing that the Secretary of Labor, acting through the Children's Bureau and in cooperation with federal, state and local agencies and qualified institutions of higher education, shall (1) make studies of the health and physical status of children of school ages, (2) make studies of the facilities and services offered by schools for the correction of physical defects of children of school ages and (3) recommend the use of and demonstrate in representative urban and rural areas methods of conducting school health examinations and providing school health services. For the fiscal year ending June 30, 1946 an appropriation of $100,000 will be authorized and for each of the next two fiscal years $450,000.

Miscellaneous

Senator Pepper, Florida, for himself and Senator George, Georgia, Senator La Follette, Wisconsin, and Senator Taft, Ohio, has introduced S. 1779 proposing to authorize the Federal Security Administrator, through such officers or employees or units of the Federal Security Agency as he may designate, to assist the several states, their political subdivisions and nongovernmental organizations (1) to develop and carry out, particularly in areas where such measures are of importance to military or naval personnel, measures designed to prevent prostitution,

eliminate conditions contributing to sex delinquency and provide services for the rehabilitation of sex delinquents and (2) to foster cooperation in communities among law enforcement, welfare and other public and private activities for the purpose of preventing prostitution, eliminating conditions contributing to sex delinquency and providing services for the rehabilitation of sex delinquents. For the fiscal year ending June 30, 1947 an appropriation of $700,000 is to be authorized and so much as may be necessary for each fiscal year thereafter.

S. 1769, introduced by Senator McFarland, Arizona, proposes to amend the Social Security Act to provide for an increase of 35 per cent in the federal share of old age assistance, aid to dependent children and aid to the blind.

STATE LEGISLATION

Georgia

Bills Introduced.—H. R. 170 proposes a resolution to amend the state constitution to create a State Board of Health with authority over all matters relating to the health and life of the people of the state. H. 695 proposes to require both parties to a marriage to present a certificate signed by a qualified physician, licensed to practice medicine and surgery in any state or United States territory, stating that the applicant has been given an examination and is not infected with syphilis. H. 712, to amend the act relating to the licensing of pharmacists, proposes that applicants for registration shall be graduates of a high school and shall have attended a generally recognized college of pharmacy for a period of two years. H. 734 proposes that all persons between the ages of 14 and 50 should have their blood examined for syphilis by an approved laboratory test. H. 771, to amend the workmen's compensation law, proposes that verified copies of all medical reports of claimants be sent immediately to the claimant or his attorney and to the State Board of Workmen's Compensation.

Bills Passed.—H. 655, to amend the law relating to the qualifications of applicants for a license to practice nursing, passed the house January 21. It proposes to reduce from 21 to 20 the required age of the applicant. H. 732 passed the house January 21 and the senate January 26. It proposes to authorize the Board of Health to make and promulgate reasonable rules and regulations for the protection of the health and lives of inmates and patients of hospitals, sanatoriums, infirmaries, maternity homes, nursing homes and other institutions where persons are received for treatment, examination, maternity care or nursing care in the state. In connection therewith a hospital advisory committee would be established, to consist of three members appointed by the Medical Association of Georgia or its board of councilors; the total membership of the advisory committee would number fourteen.

Kentucky

Bills Introduced.—S. 56, to amend the law relating to the practice of pharmacy, proposes that applicants for a license to practice pharmacy must be citizens of the United States, must have graduated from a school or college of pharmacy recognized and approved by the Kentucky Board of Pharmacy and must submit proper affidavits showing a minimum of one year of experience in a retail pharmacy under the supervision of a registered pharmacist. H. 87 and S. 30, to amend the workmen's compensation act, propose to increase the number of persons on the medical committee of the workmen's compensation board from three to five and further propose that such committee shall include at least one surgeon and one neurologist. H. 96 proposes the creation of a Kentucky State Board of Naturopathic Examiners to examine, license and regulate persons desiring to practice naturopathy, which is defined by the bill as being "a distinct system of healing based upon its own philosophy and teachings as to the causes of disease, the prevention and cure of human illness, and the maintenance of health. It means 'Nature-Cure, or Health by Natural Methods'; it embraces the prevention, diagnosing and treating human beings with their injuries, ailments or diseases, by the use of one or more of the physiological, physical or mechanical, chemical or material, forces or agencies of nature. It is a science and art of assisting nature in elimination, maintenance, and revitalization, using all methods and modalities that will assist in removing toxins and pathologies, restoring cell vitalization and remineralization without destruction of vital force, as taught in naturopathic schools, colleges, or universities teaching courses of not less than four years of nine months each, covering not less than forty-four hundred class hours of fifty minutes each, covering a curriculum peculiar to the art and science and practice of naturopathy." The proposal would further authorize licensees thereunder to practice naturopathy in accordance with the state health laws and in conformity with the teaching of class A naturopathic schools, "embracing the use of phytotherapy (the use of herbs and the facts thereof, provided the same is not under the narcotic law), minor surgery, meaning the breaking or severing the skin or membrane, or and orificial work, obstetrics and gynecology, autotherapy and biologicals, and shall enjoy right and privileges equal to those enjoyed by other physicians practicing in this commonwealth." Licensees hereunder would be authorized to sign death certificates and execute all legal documents and certificates with the same authority as under the law members of other schools or systems of treatment may do.

Massachusetts

Bills Introduced.—H. 771 proposes that any person entitled to soldier's relief under the general laws shall have the right to procure necessary treatment by a doctor, dentist, nurse or hospital of his own choosing, and the reasonable charges made by such doctor, dentist, nurse or hospital for services rendered shall be paid by the appropriate municipal authorities. H. 782 and H. 794, to amend the law relating to recipients of old age assistance, propose that aid given shall include the reasonable amount of necessary and proper expenses for medical, hospital and other services rendered to such person. H. 844, to amend the law relating to nonprofit hospital service corporations, proposes that every corporation subject to this chapter be declared to be a charitable corporation. The existing law exempting the property of such corporation from state, county, district and municipal taxes is repealed. H. 1132, to amend the law relating to actions for personal injuries, proposes that a physician or surgeon who makes a physical or mental examination of an injured person in connection with any claim for damages for personal injuries shall be deemed to be the agent of the party for whose information the examination was made for the purpose of answering interrogatories. H. 1180, to amend the law relating to recipients of old age assistance, proposes that such assistance shall include the services of a physician of such recipient's choice if said physician meets the requirements of the Massachusetts Medical Society. H. 1339 proposes a comprehensive act relating to the regulation of animal experimentation. H. 1340, to amend the law relating to animal experimentation, proposes that whoever purchases or acquires a dog, cat or bird to be used for experimentation or multilation while alive shall keep a record and submit a report to the commissioner of public safety of each such transaction showing the source from which such animal or bird was obtained. H. 1380 proposes the establishment of a hospital clinic in downtown Boston to receive and care for veterans who require medical aid or treatment at any hour of the day or night. H. 1401 proposes that every physician, surgeon or dentist who has served for any period of time in the armed forces shall be exempt from the payment of any fee or charge otherwise payable by him under the laws of the state.

Mississippi

Bills Introduced.—H. R. 10 proposes a resolution memorializing the Congress of the United States to enact suitable and adequate legislation for the training of doctors at government expense to take care of personnel of the United States armed forces wounded in the service of the country. H. 72 proposes the creation of a four year medical school as a department of the University of Mississippi which shall be operated as a class A medical school in accordance with the "Council of Medical Education" of the American Medical Association. H. 73 proposes the creation of a Memorial Hospital Commission to establish a War Memorial Hospital which shall maintain and operate a cancer clinic and perform research work in cancer and other diseases. H. 106, to amend the law relating to the operation of a Mississippi State Insane Hospital, proposes that neither the superintendent nor any other person legally participating in the execution of the treatment and regimen prescribed for a

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patient therein shall be liable either civilly or criminally on account of said participation. H. 276 proposes that all residents of the state on reaching his or her sixteenth birthday shall submit to a medical examination as to the absence or presence of venereal disease. The medical examination shall be made by any licensed physician selected by the person to be examined. S. 45 proposes the creation of a four year medical school and a university hospital to be built, established, maintained and operated in the state of Mississippi, the school to maintain standards of schooling and teaching which shall be in accordance with the standards approved by the Council on Medical Education and Hospitals of the American Medical Association and of the Association of American Medical Colleges. The proposal would also create a "Physicians Advisory Board" consisting of five physicians, who shall be members in good standing of the Mississippi State Medical Association. S. 90 proposes to authorize the State Board of Health to maintain injunctive procedures to enjoin and profit any person from the practice of any profession required to be licensed by said board when such person is practicing said profession without having first obtained such license.

Bills Passed.—S. 80 passed the Senate January 29. It proposes to require applicants for a marriage license to present a certificate showing freedom from venereal disease. The certificate may be executed by an active licensed physician in Mississippi, or a physician licensed to practice in any or all of the other states of the United States, or the District of Columbia, or by a commissioned medical officer on active duty in the armed forces of the United States, or by a medical officer of the United States Public Health Service. When the applicant is unable to pay for such certificate, the certificate may also be executed by any full time county health officer in the state who is a regular graduate of medicine and is licensed to practice medicine in Mississippi.

Missouri

Bills Introduced.—H. 831, to amend the law relating to the appointment of deputy state commissioners of health, proposes that the county courts of any county be authorized to appoint as a deputy state commissioner of health a duly licenced qualified physician. The existing law requires only the appointment of a reputable physician. S. 359 proposes the establishment within the department of education of a division of registration and examination to coordinate the work of existing boards of registration and examination, including the state board of medical examiners, the state board of chiropractic examiners and the state board of osteopathic registration and examination.

New York

Bills Introduced.—A. 326, to amend the hospital lien law, proposes that, where an injured person receives treatment, care and maintenance in a hospital ward, cost rates shall for the purposes of this section be deemed equivalent to the scheduled rates currently approved by the industrial commissioner and the superintendent of insurance for cases under the workmen's compensation law. The lien of the hospital shall not extend to personal services rendered by a physician or surgeon, however. A. 470 and S. 470, to amend the labor law, propose that the illness or disability of a claimant causing his unemployment must be certified by a physician or surgeon duly licensed to practice in the state of New York. S. 434, to amend the law in relation to maternal and child health, proposes that the commissioner of health be required to act in an advisory and supervisory capacity in matters pertaining to the safeguarding of motherhood, the saving of infant life and the prevention of the diseases and defects of childhood. S. 469, to amend the unemployment insurance law, proposes that the sickness or accident disability causing the claimant to be unemployed shall be certified under oath by a physician or surgeon duly licensed to practice in the state of New York. S. 709, to amend the insurance law, proposes that the superintendent of insurance be authorized to withhold his approval of an accident insurance or health insurance form if any such form or any application, rider or endorsement to be used in connection therewith contains provisions which are unjust, unfair, inequitable, misleading or contrary to law or the public policy of the state.

Virginia

Bills Introduced.—H. 39 and S. 45 propose that the governor be authorized to execute insurance contracts for group hospitalization and surgical benefits for state employees who become participating members of the plan. H. 58 and S. 52 propose that the state department of health be authorized to establish a program for the medical examination of all children in the public free schools, such examination to be sufficient to disclose the health, physical condition and defects of such public school children. H. 66 proposes that the state department of health be directed to establish a program for the education of the citizens of the state engaged in agriculture and industry of the value and benefits of prepaid hospital and medical care and to appropriate the sum of ten thousand dollars for such program. S. 51, to amend the law relating to marriage and divorce, proposes that it shall be sufficient grounds for divorce when either spouse has been adjudicated insane, committed to and continuously confined for five or more years in one or more institutions for the confinement and treatment of insane persons and is shown to be incurable. The divorce would not be granted until after a thorough examination of the insane defendant by three physicians of recognized ability in mental diseases has been made. S. 64 proposes the creation of a Commission on Post-Mortem Examinations and the appointment of a Chief Medical Examiner who shall be a skilled pathologist and eligible to be licensed as a Doctor of Medicine. The Chief Medical Examiner would be provided with an office and laboratory having adequate professional and technical personnel and physical facilities for the conduct of postmortem examinations and of such pathologic, bacteriologic and toxicologic investigations as may be necessary or proper. The section dealing with the appointment of coroners would provide that each coroner shall be appointed from a list of two or more licensed doctors of medicine submitted by the component medical society of the county or city in which the appointment is to be made. S. 72 proposes to authorize the state board of public welfare to provide reasonable rules and regulations for the construction, maintenance and operation of boarding homes, homes for the aged and other similar homes, the word "home" meaning "any place, establishment or institution operated or maintained for the maintenance or care of two or more aged, infirm, chronically ill or incapacitated persons." The proposal would exempt from its provisions any hospital, nursing home, maternity home, children's home or other home or institution which is already or may hereafter be subject to regulation by the board. S. 73 proposes the creation of a sanatorium for white residents affected with nervous diseases, mental diseases, alcoholism or drug addiction, to receive modern sanatorium care and treatment.

Coming Medical Meetings

Annual Congress on Medical Education and Licensure, Chicago, Feb. 11-12. Dr. Victor Johnson, 535 North Dearborn St., Chicago, Secretary.

American Association of Anatomists, Cleveland, April 4-6. Dr. Eliot R. Clark, University of Pennsylvania School of Medicine, Philadelphia 4, Secretary.

American Association of Pathologists and Bacteriologists, Chicago, March 8-9. Dr. Howard T. Karsner, 2085 Adelbert Road, Cleveland, Secretary.

American Orthopsychiatric Association, New York, Feb. 14-16. Dr. Nina Ridenour, 1790 Broadway, Room 916, New York 19, Secretary.

American Physiological Society, Atlantic City, March 11-15. Dr. Wallace O. Fenn, 260 Crittenden Blvd., Rochester 7, New York, Secretary.

American Society for Experimental Pathology, Atlantic City, March 11-15. Dr. Harry P. Smith, 630 W. 168th St., New York 32, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Atlantic City, March 11-15. Dr. Raymond N. Bieter, University of Minnesota Medical School, Minneapolis, Secretary.

American Surgical Association, Hot Springs, Va., April 2-4. Dr. Warfield M. Firor, Johns Hopkins Hospital, Baltimore 5, Secretary.

Chicago Medical Society Annual Clinical Conference, Chicago, March 5-8. Dr. Warren W. Furey, 30 North Michigan Ave., Chicago 2, Secretary.

Dallas Southern Clinical Society, Dallas, Texas, March 18-21. Dr. John G. Young, 1719 Pacific Avenue, Dallas 1, Director of Clinics.

Federation of American Societies for Experimental Biology, Atlantic City, March 11-15. Dr. D. R. Hooker, 19 West Chase Street, Baltimore 1, Secretary.

Medical Library Association New Haven, Conn., March 25-27. Miss Frida Pliefke, 2000 Medical Arts Bldg., Minneapolis 2, Secretary.

Missouri State Medical Association, St. Louis, March 24-26. Dr. Ralph L. Thompson, 634 N. Grand Blvd., St. Louis 3, Secretary.

National Conference on Medical Service, Chicago, February 10. Dr. Cleon A. Nafe, 822 Hume-Mansur Bldg., Indianapolis 4, Secretary.

Southeastern Surgical Congress, Memphis, Tenn., March 11-13. Dr. Benjamin T. Beasley, 45 Edgewood Ave. S.E., Atlanta 3, Georgia, Secretary.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST; SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Los Angeles Association Plans Addition to Building.—The Los Angeles County Medical Association plans to build an addition to provide much needed stack room facilities for the library and office and community rooms for the association itself.

New Section on General Practice.—On January 24 the organization meeting of the section on general practice of the Los Angeles County Medical Association was held under the chairmanship pro tem of Dr. Eric A. Royston and secretaryship pro tem of Dr. H. Vern Soper, both of Los Angeles.

Hospital Staff Cooperates to Reduce Accidents.—On January 15 the medical staff of the San Antonio Community Hospital, Upland, met in conference with law enforcement officials of the West End of San Bernardino County, the morticians and ambulance owners and judges of the various courts and representatives of the press to discuss and make recommendations of ways and means to reduce materially the heavy unnecessary traffic fatalities. The conference was the result of the recognition that traffic deaths and personal injuries had increased since V-J day, Aug. 14, 1945. A committee of three was named to draw up a resolution carrying recommendations to reduce these accidents, and copies were sent to local and national authorities as well as to the members. The resolution urges the following:

More traffic officers and greater frequency of patrol.

Driver educational program and (*a*) educational program in junior and senior high schools, with "behind the wheel" actual instruction; (*b*) prerequisite training and certification before issuance of driver's license; (*c*) physician's approval of ability of driver with physical disability.

All drivers involved in accidents to be reexamined within thirty days or driver's license revoked:

(*a*) Immediate revocation of licenses of all drivers involved in accidents resulting in personal injury or death, pending reexamination.

(*b*) Drivers apprehended operating a motor vehicle without a license to be incarcerated in county jail for a term of not less than ninety days and during such incarceration, at the discretion of the department of motor vehicles, perform such duties in the general program to enhance the safety of our highways.

Heavier and uniform fines and sentences along with impounding of cars on all violations of drunken driving and/or reckless driving and/or driving without due caution or any wanton disregard of safety on the highway.

Improved engineering on all main highways; to be at least four lane divided highways:

(*a*) Immediate survey of dangerous intersections and removal of all obstructions impairing visibility.

(*b*) More frequent location checks on mechanical equipment and driving ability by all traffic officers.

(*c*) Adequate flood lighting of intersections, particularly those used by pedestrians, and all main intersections.

COLORADO

Midwinter Postgraduate Clinics.—The eleventh annual midwinter postgraduate clinics conducted by the Colorado State Medical Society will be held at Denver hospitals and the Shirley Savoy Hotel, February 27-March 1. This will be the first revival of the Denver midwinter clinical session since 1942, when war conditions forced its indefinite postponement. Among the speakers will be:

Dr. Edward L. Compere, Chicago, The Treatment of Compound Fractures.

Dr. Bruce K. Wiseman, Columbus, Ohio, Hypersplenism and the Blood Dyscrasias.

Dr. Henry G. Poncher, Chicago, Fever as a Diagnostic Problem in Infants and Children.

Dr. Frederic E. B. Foley, St. Paul, The Part of the General Practitioner in the Management of Vesical Neck Obstruction.

Dr. M. Edward Davis, Chicago, The Modern Management of Placenta Previa.

Dr. J. Dewey Bisgard, Omaha, The Cancer-Ulcer Problem of the Stomach.

Col. John B. Grow, M. C., Denver, The Modern Approach to Neoplasms of the Chest.

DELAWARE

Thirty Years as Editor.—Dr. W. Edwin Bird, Wilmington, observed his thirtieth anniversary as editor of the *Delaware State Medical Journal* with the December issue. In editorial comment the journal states that Dr. Clarence A. Smith, Seattle, of *Northwest Medicine* has served for forty-two years and Dr. Holman Taylor, Fort Worth, Texas, of the *Texas State Journal of Medicine* for thirty-six years.

ILLINOIS

Personal.—Dr. Ruth E. Church, who has been medical director of the District Health Unit Number 7 at Washington, Iowa, for several years, has resigned to become director of the McDonough-Fulton Bi-County Health Department, with headquarters in Macon and Canton, effective December 1.

Chicago

Personal.—Dr. Robert Neubaur, head of the medical division of the Yugoslav Red Cross, was guest at a dinner on January 25 given by the Chicago chapter of the American Committee for Yugoslav Relief.——Albert L. Raymond, Ph.D., formerly a member of the staff of the Rockefeller Institute for Medical Research and recently director of research of G. D. Searle and Company, has been appointed vice president in charge of research of the company.

Society News.—Dr. Herbert S. Ratner, Hinsdale, Ill., director of the student health service, Loyola University School of Medicine, lectured at the Marquette University School of Medicine, Milwaukee, on the "Extramedical Element in the Therapeutic Decision."——John L. Bach, associate director of public relations, American Medical Association, addressed the Lions Club, Michigan City, Ind., January 23 on "Fifty Years of Medical Progress."——At the recent meeting of the Chicago Tuberculosis Society Drs. Jacob J. Mendelsohn was elected president, Arthur S. Webb, Wheaton, vice president and Hugo T. Cutrera secretary-treasurer.

New Appointments at Illinois.—Dr. Douglas A. MacFadyen and Dr. George M. Hass have been appointed Rush professor of biochemistry and Rush professor of pathology, respectively, in the Rush-Presbyterian Hospital division of the University of Illinois College of Medicine. Dr. MacFadyen previously was chief of the division of chemistry and physics of the Army Medical Center in Washington and Dr. Hass was chief of the department of pathology of the School of Aviation Medicine, Randolph Field, Texas, both with the rank of major. The appointments constitute an important step in the achievement of an expanded research and teaching program involving the basic medical departments of the Rush-Presbyterian Hospital division.

INDIANA

Health Center Named for Dr. Morgan.—The new health center at Flanner House has been named in honor of the late Dr. Herman G. Morgan, in recognition of his thirty-five years' service as secretary of the Indianapolis Board of Health (THE JOURNAL, Sept. 8, 1945, p. 140).

Personal.—Dr. Miles F. Daubenheyer, Holton, has been named superintendent of the Muscatatuck State School, Butlerville, succeeding Dr. Otis R. Lynch, who resigned to become superintendent of the Richmond State Hospital.——Dr. James M. Burk has resigned as secretary of the Decatur Board of Health, effective January 1.——Dr. Richard N. Washburn, Rensselaer, has been appointed coroner of Jasper County to fill the unexpired term Dr. Merle D. Gwin, who has moved to Florida.

School of Health and Physical Education.—Indiana University, Bloomington, has announced the establishment of a school of health, recreation and physical education as the first step in the university's postwar development program. The school will have four departments: physical education offering service courses in all schools of the university; health and safety, giving courses in these subjects together with a program of research and graduate study; recreation, coordinating all campus activities and student intramural sports, with courses designed to train directors of community and school recreation programs, and professional physical education, offering technic courses for teachers, also with research and graduate study programs.

Division of Adult Hygiene and Geriatrics.—Dr. William F. King, Indianapolis, formerly health commissioner of Indiana, is director of the recently created division of adult hygiene and geriatrics of the state department of health. The new division was authorized at the last session of the Indiana general assembly (THE JOURNAL, March 17, 1945, p. 663). The *Journal of the Indiana State Medical Association* points out that to be concerned with factors of aging and problems of the aged is a relatively new and untried activity of the public health administration. It stated that the number of men and women in Indiana who have attained the age of 60 and over is in excess of three hundred and fifty thousand. The number in this age group in the continental United States is estimated at above thirteen million. Within the last census

decade 1930 to 1940 there was an increase in the number of persons 65 years of age and over of 35 per cent, while in contrast the total population increase was but 7.2 per cent in the same period.

IOWA

Personal.—Effective January 1, Dr. Everett M. George, Des Moines, who recently returned from service with the U. S. Navy, assumed the position of editor of the *Journal of the Iowa State Medical Society*. He succeeded Dr. Lee F. Hill, Des Moines, who had held the position for the past nine years.

Course on Tropical Diseases.—A second laboratory training course on parasites of malaria, amebiasis and tropical diseases was recently held at the State Hygienic Laboratory, Iowa City. The course was sponsored by the State University of Iowa College of Medicine, Iowa City, and the Iowa State Department of Health in cooperation with the U. S. Public Health Service. The first course of this kind took place July 23-28, 1945. Those in attendance at the two courses totaled fifty-eight, including fifty-four laboratory workers and four physicians representing thirty-one counties and thirty-five hospitals in all parts of the state.

MASSACHUSETTS

The Cutter Lecture.—Dr. Donald Hunter, physician to the London Hospital, London, recently gave the Cutter Lecture on Preventive Medicine at the Harvard Medical School, Boston, on "Research in Industrial Medicine in Great Britain at War."

Study of Dental Caries.—The Dental Bureau of the Massachusetts Department of Public Health, Boston, in preparation for conducting a research program in the control of dental caries, is making a survey to determine the incidence of caries among children by age groups and to determine the availability of sufficient dentists to cope with the existing problem. The fluoride control of all public water supplies in the state has already been determined and in only one town, Farumsville, was as much as 1 part per million of sodium fluoride (1.3 parts per million) found. In all other public water supplies the amount of sodium fluoride was near 0.2 part per million. These data will be used as the basis for the proposed study, which will investigate the control of dental caries by utilizing fluorides in public water supplies, in prophylactic pastes and mouth washes, in pastilles and lozenges, in pills and in topical applications. In each community where the study is being conducted 250 children are participating, and a like number are serving as the control.

MICHIGAN

Personal.—Dr. Louis P. Munger, Hart, recently completed fifty years in the practice of medicine.——Dr. Sylvester E. Gould, Eloise Hospital, Eloise, has been appointed editor in chief of the *American Journal of Clinical Pathology* to succeed Dr. Israel Davidsohn, Chicago.

Society Honors Members Who Served in War.—The Saginaw County Medical Society gave a dinner recently to welcome home its members who have been in military service. Dr. Alexander R. McKinney, Saginaw, was toastmaster at the banquet, at which wives of members and widows of former members were guests.

Meeting on Cancer.—The Genesee County Medical Society will devote its meeting March 20 to a symposium on cancer, to be presented by:

Dr. Louis E. Phaneuf, Boston, Cancer of the Uterus.
Dr. Paul A. O'Leary, Rochester, Minn., Cutaneous Malignancy.
Dr. Charles B. Huggins, Chicago, Cancer of the Genitourinary System.
Dr. Frederick A. Coller, Ann Arbor, Cancer of the Stomach.
Dr. Frank E. Adair, New York, Cancer of the Breast.

NEW JERSEY

New Director of Preventable Disease.—Dr. Leonid S. Snegireff, Trenton, has been appointed director of the bureau of preventable diseases of the New Jersey State Department of Health, according to the *Bulletin* of the National Tuberculosis Association. The new bureau includes divisions covering tuberculosis and venereal disease control, maternal and child health, preventive medicine, industrial and dental health and health education. Dr. Snegireff was formerly medical assistant in the department of health.

Brandenburg Arrested on Abortion Charge.—A ring charged with performing illegal operations was broken up January 18 when Bergen county and state police raided a farm house on a 25 acre estate in Park Ridge and arrested six persons. The New York *Times* reported that, according to Michael Orrechio, detective chief of Bergen County, the ring was headed by Dr. Leopold W. A. Brandenburg, Union City, who has a long record of arrests (THE JOURNAL, Sept. 30, 1944, p. 310). Among those arrested with Dr. Brandenburg were Mrs. Sadie Strohmeyer, North Plainfield, who was convicted on abortion charges in 1939 and who was on a five year probation. The bail for Brandenburg was set at $25,000 and for Mrs. Strohmeyer at $10,000. The other persons' bail was set at $5,000 each. Dr. Brandenburg has been mixed up in a number of irregularities, such as violation of narcotic laws, possession of stolen goods and harboring a fugitive by removing finger prints.

NEW YORK

Dr. Conway Ends Thirty-One Years' Service.—Dr. John A. Conway, district health officer with headquarters in Hornell, resigned January 1, concluding thirty-one years' service in the state department of health. Dr. Conway was one of the first six physicians appointed on the department staff in 1914 under the title of "district sanitary supervisor," a position corresponding to the present "district state health officer." He is the only one of the original appointees who has served continuously in the same position to the present time. For many years he has served the counties of Allegany, Chemung and Steuben from headquarters in Hornell. At one time he was president of the Steuben County Medical Society.

Rabies Consultant Appointed.—Alexander Zeissig, D.V.M., has been appointed veterinary consultant on rabies on the staff of the division of communicable diseases of the state department of health. In this capacity he will organize a statewide program for the control of rabies, including preventive measures for application in advance of the appearance of the disease. Dr. Zeissig in 1930 was awarded a fellowship in medicine by the National Research Council and studied for one year at the medical school at Heidelberg, Germany. Since his return to this country in 1931 he has been associated continuously with the New York State Veterinary College, first as assistant professor and later as associate professor of bacteriology.

New York City

The Biggs Memorial Lecture.—Laurence H. Snyder, Sc.D., professor of medical genetics, Ohio State University College of Medicine, Columbus, will give the annual Hermann M. Biggs Memorial Lecture at the New York Academy of Medicine, April 4. His subject will be "Medical Genetics and Public Health."

Society Honors Past Presidents.—The Medical Society of the County of Kings will hold a dinner February 20 in the Hotel St. George, Brooklyn, to honor its immediate past presidents. The society voted the annual dinner honoring the retiring presidents in 1941 but discontinued the practice during the war. The physicians to be honored are Drs. William C. Meagher, John J. A. Gainey, Leo S. Schwartz and Joseph Tenopyr, all of Brooklyn. They will be given medals and scrolls. Dr. Morris Fishbein, Editor of THE JOURNAL, will discuss "Medicine and the Postwar World."

Student Society.—At a recent meeting of the Contin Society, honorary scholastic society of the New York Medical College, Flower and Fifth Avenue Hospitals, Dr. Thomas H. Evans, research professor of anatomy, was elected to honorary faculty membership. Senior students chosen for membership include Lesley M. Warshaw, Julius Stein, Sidney J. Peck, Robert Maxfield and Ednita P. Bernabeu. Undergraduates chosen from the junior class were Peter Laderman, Burton L. Wise, Herbert M. Eskwitt, Morton P. Lazar, Max Cohen and Norman Ackerman. Mr. Ackerman is secretary of the Contin Society.

Friends of Medical Research.—A group known as the Friends of Medical Research has been organized to inform the public about animal experimentation and its contribution to public health. The organization was launched under the auspices of the New York Academy of Medicine, and Dr. Simon Flexner has been named honorary president. The first efforts of the new organization are to be directed toward the defeat of the DiCostanzo-Davidson bill in the state legislature to make research work with dogs unlawful. It is intended that the statewide organization shall be coordinated with similar ones in every county of the state, one of which has already been organized in Rochester and Monroe County.

Robert Potter Teaches First College Course in Science Reporting.—Robert D. Potter, science editor of the *American Weekly* and former president of the National Association of Science Writers, will teach the first college course in science reporting and editing at New York University, it was announced January 24. The course has been organized to meet a demand

for trained science writers brought on by the interest in scientific subjects which has grown out of the war. It is the culmination of several months' planning by the National Association of Science Writers and will be offered on Wednesday evenings from 8 to 10 during the spring term beginning in February. The needs of different mediums, an examination of sources and tools needed by the science writer, and a discussion of science terminology will feature the course. Each student will be given regular science writing assignments from learned journals and will have his articles discussed and edited by the instructor. A critical discussion of science stories which reach an editor's desk will be held at each class session. Mr. Potter was formerly with the New York *Herald Tribune* and Science Service and was acting chairman of the department of general science at the New York University School of Commerce during the war.

Internal and Psychosomatic Medicine.—Cornell University announces a project in internal medicine at the New York Hospital designed to deal clinically and experimentally with psychosomatics. The principal objects are to develop a practical method of dealing with ambulatory clinic patients who suffer from symptoms related to their emotional states and life situations, to engage in experimental study of the mechanisms involved in illness of this nature and to train especially able young physicians in experimental methods and a critical psychosomatic approach to the care of the sick. About half time will be spent in the diagnosis and management of patients and half time in research dealing mainly with mechanisms underlying symptoms. The project will be under the direction of Dr. Harold G. Wolff, assisted by Dr. Stewart Wolf, internist, Dr. Herbert S. Ripley Jr., a psychiatrist, and six fellows. Fellows will be appointed for a period of one year with the expectation of serving for two or more. Candidates for fellowship, who will receive a salary of $2,500 a year for the first year, should have had at least two years in internal medicine and have given evidence of a psychiatric orientation. They need not necessarily have had experience in research but must have a serious interest in investigation, energy and curiosity. Prospective candidates should arrange for a personal interview through Dr. David P. Barr, New York Hospital, 525 East Sixty-Eighth Street, New York.

NORTH CAROLINA

Portraits of Physicians.—Portraits of Drs. Richard H. Whitehead and Charles S. Mangum were presented to the University of North Carolina School of Medicine December 2. Dr. Whitehead was dean of the medical school from 1891 to 1905, when he went to the University of Virginia; he died in 1916. Dr. Mangum was on the medical school faculty from 1896 until his death in 1939, serving as dean from 1933 to 1937. Dr. George L. Carrington, Burlington, president of the University Medical Alumni Association, presided at the ceremony, which took place in the library of the medical school.

OHIO

Changes in Health Personnel.—Dr. Arthur B. Ream, Batavia, has resigned as health commissioner of Clermont County to engage in private practice in Mechanicsburg.—— Dr. George A. Poe, Port Clinton, is the new health commissioner of Ottawa County.

Isaac Harris Named Professor Emeritus.—Dr. Isaac B. Harris, professor of clinical surgery, Ohio State University College of Medicine, Columbus, has retired with the title of emeritus professor. Dr. Harris graduated at Starling Medical College in 1900, joining the faculty in 1904 after finishing advance study at the Harvard Medical School and the New York Postgraduate Medical School. He has continued on the staff steadily since then. The present name of the Starling College is the Ohio State University College of Medicine.

Cleveland Clinic Observes Twenty-Fifth Anniversary.—The Cleveland Clinic will celebrate its twenty-fifth anniversary, February 24-27. The opening will be held in the auditorium of the Cleveland Medical Library. A "Refresher Course in Treatment," consisting of a series of lectures and demonstrations, will be given at the clinic. In connection with this course Edmund N. Cowdry, Ph.D., St. Louis, will address a dinner meeting on "Precancerous Lesions." Dr. Bertrand E. Lowenstein, instructor in the department of physiology of Yale University School of Medicine, has joined the division of research at the Cleveland Clinic and will carry on genitourinary investigations under the terms of the Packard Endowment gift, it is reported.

OKLAHOMA

New Executive Secretary.—E. G. Green, educational director of the Oklahoma County Health Association, Oklahoma City, has been appointed acting executive secretary of the association for a minimum of one year. Arthur H. German, who was executive secretary for seven years, resigned to become consultant to the fund raising department of the Midwest division of the American Red Cross with offices in St. Louis. Mr. Green was a member of the original board of the old Tuberculosis Society of Oklahoma City, which was a forerunner of the Oklahoma County Health Association, chartered with its services expanded April 22, 1943.

OREGON

Course in Ophthalmology.—The sixth annual spring postgraduate course in ophthalmology and otolaryngology will be held in Portland, April 15-20, under the auspices of the Oregon Academy of Ophthalmology and Otolaryngology and the University of Oregon Medical School, Portland. Guest speakers will include Drs. Algernon B. Reese, professor of ophthalmology at Columbia University College of Physicians and Surgeons, New York, and Gabriel Tucker, professor of bronchoscopy and esophagology at the University of Pennsylvania School of Medicine, Philadelphia.

PENNSYLVANIA

Change in Health Board Secretary.—Dr. Charles V. Hogan, for fifteen years a member of the Pottsville Board of Health, has been named secretary to succeed H. J. Herbein, D.D.S., who resigned December 1 after holding the position about thirty-three years. Dr. Hogan has served as member and president of the board for fifteen years.

Philadelphia

The Ulrich Memorial Lecture.—Dr. Thaddeus L. Montgomery, professor of obstetrics and gynecology, Temple University School of Medicine, gave the second annual George A. Ulrich Memorial Lecture February 6 at Jefferson Medical College. The lecture, which was entitled "The Placenta," is sponsored by the Alpha Kappa Kappa medical fraternity, of which John D. Bealer is corresponding secretary. The lecture is named for Dr. George A. Ulrich, who died in 1944. He had been clinical professor of obstetrics at Jefferson and had graduated there in 1901.

Mental Hygiene Lectures—Cancer Seminars.—On January 28 the Philadelphia County Medical Society launched a series of public lectures on various phases of mental hygiene. The initial speakers were Drs. James J. Waggood on "The Emotional Needs of the Infant and Young Child," and Ralph M. Tyson on "The Emotional Factors During Illness in Children." The society gave the first in a series of four cancer seminars January 24 on Cancer of the Breast; others in the series are Pelvic Cancer, February 21, Cancer of the Esophagus and Stomach, March 21, and Cancer of the Colon, April 18.

Fifty Years of Practice.—At a luncheon meeting of the first councilor district of the Medical Society of the State of Pennsylvania, January 8, at the Philadelphia County Medical Society, the following members of the county medical society received framed certificates from the state society in recognition of having been in the practice of medicine for a period of fifty years: Drs. W. Wayne Babcock, Richard D. Burke, Cunningham P. Clark, Clarence H. Fritz, Alfred Gordon, Edwin A. Heller, Daniel J. McCarthy, Louis H. Mutschler, Herbert Old, Charles S. Raue, George N. Richmond, Thomas T. Thomas, Joseph P. Walsh, Rachel R. Williams, and Christian G. Yaeger, Elizabeth L. Pickett, Aldan, Pa., and Henry Archer Cleaver, Wilmington, Del.

TEXAS

Gynecologic Survey of Women in State Institutions.—A comprehensive gynecologic survey of women in Texas state institutions is being organized under the direction of Dr. Willard R. Cooke, professor of obstetrics and gynecology at the University of Texas Medical Branch, Galveston, and his associate, Dr. John D. Weaver. This survey is being made in cooperation with the state board of control with Judge Weaver Baker as chairman. It is supported by a three year grant of $20,000 from the Lilly Research Laboratories of Indianapolis.

Grants for Research.—The Lilly Research Laboratories, Indianapolis, have made a grant of $2,500 to the University of Texas Medical Branch, Galveston, to establish a training fellowship in tissue culture, with special reference to the

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reticuloendothelial system. The work will be under the direction of Charles M. Pomerat, Ph.D., professor of anatomy and director of the tissue culture laboratory. The National Foundation for Infantile Paralysis has made a grant of $3,500 to the medical branch to support the studies of Ardzroony Packchanian, Ph.D., director of the laboratory of microbiology, on virus transmission in small animals in order to try to devise a rapid diagnosis procedure and to assist in screening tests in therapy.

WASHINGTON

Surgical Society Resumes Activities.—On November 7 the Spokane Surgical Society held its first postwar meeting and voted to hold its usual annual meeting in April. Meetings of the society were suspended during 1942 and 1944 and the spring of 1945.

Pediatric Society Changes Name.—The Seattle Pediatric Society recently changed its name to the Puget Sound Pediatric Society to include in its membership physicians in wider territory than had previously been possible. Officers are Homer T. Clay, Tacoma, president; Walter B. Seelye, Seattle, vice president, and Ward B. Chesley, Seattle, secretary-treasurer.

GENERAL

Orthopsychiatric Meeting.—The American Orthopsychiatric Association will hold its twenty-third meeting at the Hotel New Yorker, February 14-16, under the presidency of Dr. Norvelle C. LaMar, New York. The program has been divided into discussions on Service Problems, Counseling, Treatment of Delinquents, Sociopsychiatric Problems, Group Psychotherapy, Psychoses and Schizophrenia in Childhood, Industrial and Personnel Problems, Psychologic Considerations, Clinical and General Problems and Childhood Emotional Problems.

Robert Page Named Medical Director of Standard Oil Company.—Dr. Robert C. Page, New York, a medical officer in the Army Air Forces during World War II and assistant medical director of the Standard Oil Company of New Jersey, has been appointed general medical director of the company, succeeding Dr. Willard J. Denno, New York, chief medical officer since 1918. Dr. Denno, who developed the company's medical department from an office with one part time physician to a worldwide organization having eleven hospitals and more than 150 physicians and 1,500 nurses and attendants, helped Jersey Standard to become one of the most advanced companies in the field of industrial medicine. He will continue with the company as medical consultant. Dr. Alfred Gage, New York, an assistant medical director, will be in charge of medical service and advice for affiliated companies in Latin America.

Lasker Award Goes to Physicians.—On January 23 the $500 Albert and Mary Lasker Foundation Awards were presented to Dr. Irl C. Riggin, Richmond, Va., health commissioner of Virginia, and Dr. Robert L. Dickinson, New York, gynecologist. The awards are given for the most significant contribution to research in human fertility and for meritorious public health service. According to an announcement Dr. Riggin led Virginia in becoming the seventh state in the union to make planned parenthood services available as part of the state's public health program of maternal care. Dr. Dickinson, as organizer of the National Committee on Maternal Health, has pioneered in fundamental research in the medical aspects of human fertility and its control. The fertility award will be given in honor of the late Dr. Hannah M. Stone, first medical director of the Margaret Sanger Research Bureau, co-author with Abraham Stone of the "Marriage Manual." The public health award will be in honor of Mrs. Margaret Sanger, founder of the birth control movement and at present honorary chairman of the federation.

Resolutions Adopted by Academy of Pediatrics.—At its annual meeting in Detroit, January 15-18, the American Academy of Pediatrics, after careful consideration of proposed legislation in Congress as it relates to child health services, reaffirmed its resolution as adopted at its 1939 session, namely:

> That the American Academy of Pediatrics, regarding the provisions for maternal and child welfare, favors the use of public funds to provide such services to those groups of the population unable to pay for medical services, to the end that the standards of medical care may be maintained at a high level among such groups.

The academy indicated that it does not favor the use of federal funds for those able to provide good medical care from their own sources and directs the attention of those considering proposed legislation to its fact finding study of child health services now in progress, which at its conclusion should assist in the development of sound programs at state levels based on demonstrated needs (THE JOURNAL, February 2, p. 298). Pending the completion of this study, it is recognized that urgent needs exist in some states that should be met in the immediate future. To this end the academy recommends that additional federal funds be made available for grants-in-aid to the states under existing maternal and child health and crippled children's programs of title V of the Social Security Act. The academy also listed specific criticisms of S. 1318, citing this for its belief that the maternal and child welfare act of 1945 does not represent the best form of legislation for the purpose for which it was written. At the recent meeting Dr. Lee F. Hill, Des Moines, Iowa, was named president-elect of the academy and Dr. Jay I. Durand, Seattle, was inducted into the presidency. Dr. Clifford G. Grulee, Evanston, was reelected secretary-treasurer.

Appointments to Advisory Cancer Council.—Drs. Robert S. Stone, San Francisco, and Charles B. Huggins, Chicago, have been appointed for three year terms on the National Advisory Cancer Council, succeeding Albert B. Hastings, Ph.D., Boston, and Dr. James B. Murphy, New York, whose terms have expired. Dr. Stone is professor of roentgenology at the University of California Medical School, Berkeley. Dr. Huggins, who is professor of surgery (urology) at the University of Chicago School of Medicine, has just been named professor of urology and head of the department at Johns Hopkins University School of Medicine (THE JOURNAL, January 26, p. 231). The National Advisory Cancer Council is composed of six members in addition to the Surgeon General of the U. S. Public Health Service, who is chairman ex officio. It serves as an advisory body to the Surgeon General in the direction of the work of the National Cancer Institute. The law establishing the council provides that two members shall be appointed each year according to the council's membership arrangement. Other council members are Dr. George M. Smith, Pine orchard, Conn., research associate in anatomy, Yale University School of Medicine, New Haven, and medical director, of the Anna Fuller Fund for Cancer Research, executive director of the council; Andrew C. Ivy, professor of physiology, Northwestern University Medical School, Chicago; Frank E. Adair, New York, Memorial Hospital for the Treatment of Cancer and Allied Diseases, and Sherwood Moore, director of the Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis.

New Program on Crippling Diseases Affecting Children.—A nationwide five point program to expand and accelerate its fight against all crippling diseases affecting children will be set into action at once by the Shriners of North America, it was announced in New York recently. The new program has been developed through a series of meetings sponsored by the Shriners' Imperial Council. The five phases of the new plan are:

> The granting of scholarships, to be known as the Fellowships of the Shriners' Hospitals for Crippled Children, in orthopedic surgery to outstanding, qualified medical students. An initial yearly appropriation of $7,500 has been set aside. Three scholarships of $2,500 each will be made in 1946 for training in three universities, soon to be named.
>
> An annual appropriation of $3,750, to be granted for scholarships in orthopedic nursing. These nurses, in turn, will instruct and give encouragement to other nurses interested in specializing in the crippled children's field.
>
> The establishment of a research project to probe further the sources, methods of treatment and prevention of all crippling diseases attacking children.
>
> The expansion of present facilities and equipment of the fifteen Shriners' hospitals now in operation and establishment of new hospitals in other localities.
>
> The establishment of convalescent homes in connection with all Shriners' hospitals as rapidly as possible. The installation of recreational and occupational therapy courses to assure continuing physical improvement and self development after healing has been completed.

The convalescent and occupational therapy plan is already under way at the San Francisco Hospital. The first Shriner Hospital was opened in Shreveport, La., Sept. 16, 1922. In addition to this hospital and the one in San Francisco, other hospitals are located in Minneapolis-St. Paul; Portland, Ore.; St. Louis; Montreal, Canada; Springfield, Mass.; Chicago; Philadelphia; Greenville, S. C.; Honolulu; Spokane, Wash.; Salt Lake City; Winnipeg, Canada; Lexington, Ky., and San Francisco.

CORRECTION

Brig. Gen. Raymond W. Bliss.—In a recent item under Medicine and the War it was erroneously stated that Brig. Gen. Raymond W. Bliss graduated from Harvard Medical School, Boston, in 1910. This should have read Tufts College Medical School, Boston, in 1910.

Deaths

Waller Smith Leathers ✠ prominent medical educator, died at his home in Nashville, Tenn., January 26, aged 71, of cerebral hemorrhage.

Dr. Leathers was born near Charlottesville, Va., on Dec. 4, 1874. He carried on special studies in biology, geology, mineralogy and chemistry and graduated at the University of Virginia Department of Medicine, Charlottesville, in 1895. A member of the Alpha Omega Alpha, he subsequently received many honorary degrees. He had graduate work at Johns Hopkins University, the University of Chicago, Biological Laboratory in Long Island, N. Y., and the Marine Biological Laboratory, Woods Hole, Mass., as well as at Harvard Medical School. In 1896 Dr. Leathers began his active teaching career as a member of the department of chemistry at the Miller School of Virginia, subsequently going to the University of South Carolina as professor of biology. In 1899 he went to the University of Mississippi as professor of biology, later serving as professor of physiology and professor of physiology and materia medica. In 1903 he assisted in the organization of the medical school at the University of Mississippi, subsequently serving as its dean.

Joining Vanderbilt University School of Medicine, Nashville, in 1924 as professor of preventive medicine and public health, he became associate dean in 1927 and dean the following year, holding this position until June 30, 1945, when he retired. In 1928 he was chosen a member of the university's board of trustees.

Dr. Leathers' intense interest in medical education took him actively into related fields. He was a member of the first Basic Science Board created in Tennessee in 1943, serving as the first president. He also served as chairman of the then new state public health council. In Mississippi he had served the Mississippi State Board of Health, first in 1910 as director of public health and from 1917 to 1924 as director of public health and executive officer and member of the board. He was a member of the National Board of Medical Examiners from 1923 to 1934, serving as president from 1930 to 1934 and was elected a member at large in 1936. He had been a member of the board of scientific directors of the International Health Division of the Rockefeller Foundation from 1930 to 1933 and from 1935 to 1937, serving as a member of the advisory committee on public health of the Commonwealth Fund since 1929 and various terms on the Advisory Health Council of the U. S. Public Health Service and health and medical advisory committee of the American Red Cross.

He served the American Medical Association first in 1911 as a member of the speakers' bureau of the Council on Health and Public Instruction, as a member of the Council on Medical Service and Public Relations when it was created in 1943, resigning April 6, 1945, as secretary of the Section on Preventive Medicine and Public Health from 1920 to 1923, holding the chairmanship the following year, as a member of the House of Delegates from 1923 to 1927, and in 1938 was a member of an advisory committee to the Council on Medical Education and Hospitals.

He was a member of numerous local and national societies, serving for many years as chairman of the committee on professional education of the American Public Health Association, serving as president of the national group in 1940-1941. He was vice president of the American Association for the Advancement of Science in 1928, vice president of the Association of American Medical Colleges in 1938, and president in 1942-1943. He served as secretary of the Section on Public Health of the Southern Medical Association from 1913 to 1917 and as president, 1922-1923.

Dr. Leathers was a man of excellent judgment, of high medical ideals and a leader who inspired confidence.

Carl Ellsworth Black ✠ Jacksonville, Ill.; Chicago Medical College, 1887; born in Winchester, Ill., July 4, 1862; an Affiliate Fellow of the American Medical Association, of which he had been a member of the House of Delegates in 1904; member of the Western Surgical Association, serving as president in 1930; emeritus member of the Illinois State Medical Society and in 1904 president; president of the Morgan County Medical Society in 1927; fellow and member of the board of governors of the American College of Surgeons; served as surgeon at the Passavant Memorial and Our Saviour's hospitals and of the Chicago and Alton and the Chicago, Burlington and Quincy railroads; in 1944 presented to the Illinois State Medical Society the Carl E. Black Collection of photographs of physicians, which contained more than three thousand photographs, said to be the largest single collection in the country except for that in the office of the Surgeon General of the U. S. Army, and registered in the state museum at Springfield as the Carl E. Black-Illinois State Medical Society Collection; served as president of the Morgan County Historical Society; died January 13, aged 83, of coronary heart disease.

James Joshua Terrill ✠ Dallas, Texas; University of Texas School of Medicine, Galveston, 1902; born near Armstrong, Mo., Feb. 21, 1877; specialist certified by the American Board of Psychiatry and Neurology, Inc.; since 1943 honorary professor of neuropsychiatry at the Southwestern Medical Foundation; emeritus professor of neuropsychiatry at Baylor University College of Medicine; formerly instructor and professor of pathology at his alma mater; past president of the North Texas Medical Society and the Dallas County Medical Society; formerly secretary of the Galveston County Medical Society; member of the Southern Medical Association; served as visiting pathologist at the John Sealy Hospital and St. Mary's Infirmary; chief of laboratory, Temple Sanitarium in Temple from 1913 to 1917; a medical director of the Timberlawn Sanitarium; died October 10, aged 68, of cardiovascular renal disease and pulmonary tuberculosis.

Larue Depew Carter ✠ Indianapolis; Medical College of Indiana, Indianapolis, 1904; born in Westfield, Ind., March 17, 1880; professor of neurology and since 1914 a member of the faculty at the Indiana University School of Medicine; specialist certified by the American Board of Psychiatry and Neurology, Inc.; fellow of the American College of Physicians; served during World War I; colonel, medical reserve corps, U. S. Army, not on active duty; in 1945 appointed to the Indiana Council for Mental Health; chief consultant, "Norways" Sterne Memorial Hospital; visiting chief, department of neuropsychiatry, Indianapolis City Hospital; member of the visiting staff, department of neuropsychiatry at the Methodist and St. Vincent's hospitals; formerly on the staff of the Richmond (Ind.) State Hospital; died January 22, aged 65.

Thomas B. Bass ✠ Abilene, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1890; past president of the Taylor-Jones Counties Medical Society; member and formerly vice president of the American Psychiatric Association and the State Medical Association of Texas; served as president of the Texas Neurological Society; at one time on the staff of the North Texas Hospital for Insane in Terrell; joined the staff of the Abilene State Hospital in 1901 as first assistant physician, becoming superintendent in 1909 and serving in that capacity until 1943; physician for McMurry College; died December 22, aged 80, of chronic myocarditis.

Russell Lee Roy Allen, Daisy, Tenn.; Birmingham Medical College, 1912; member of the American Medical Association; died in Chattanooga October 13, aged 56, of heart disease.

Thomas Smith Armstrong ✠ McKeesport, Pa.; Jefferson Medical College of Philadelphia, 1903; on the staff of the McKeesport Hospital; died October 3, aged 65, of heart disease.

Emanuel Stratton Black, Williamstown, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1902; member of the American Medical Association; served during World War I; affiliated with the Veterans Administration; died October 3, aged 64, of coronary thrombosis.

Lester Belmont Bradford, Rockland, Maine; Maryland Medical College, Baltimore, 1905; during World War I a medical officer in the zone of advance; went with the Army of Occupation to Coblenz, Germany, where he remained a year after the war; at one time medical commissioner in the Balkans, helping to organize Red Cross hospitals; served on the staffs of various Veterans Administration facilities; died in Tenants Harbor September 24, aged 61, of chronic nephritis and diabetes mellitus.

Alfred H. Bullock ✠ Cushing, Iowa; Sioux City College of Medicine, 1900; died September 21, aged 71, of paralysis of the respiratory center and uremia.

Robert E. Caldwell, Waterford, Va.; Medical College of Virginia, Richmond, 1898; died in Bay Pines, Fla., October 6, aged 75, of cerebral hemorrhage.

Raymond Smith Cooper ✠ Syracuse, N. Y.; Syracuse University College of Medicine, 1910; served during World War I; on the staff of the People's Hospital; died October 7, aged 59, of hypertensive heart disease.

Allen Donaldson ✠ Carrollton, Ky.; University of Louisville Medical Department, 1898; member of the county board of health and the Radiological Society of North America, Inc.; died November 2, aged 68, of chronic myocarditis.

William B. Finney, Kennett, Mo.; St. Louis College of Physicians and Surgeons, 1890; member of the American Medical Association; served as coroner of Dunklin County; died in St. Francis Hospital, Cape Girardeau, October 27, aged 86, of senility.

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Jasper Edwin Guernsey ✠ Tacoma, Wash.; Missouri Medical College, St. Louis, 1895; for four years county coroner in Iowa; served on the staff of the Eastern State Custodial School in Medical Lake; died December 16, aged 76.

William Nelson Harrison, Upper Montclair, N. J.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1895; died October 9, aged 72, of arteriosclerosis.

Walter Lawrence Hearn, Lynn, Mass.; Harvard Medical School, Boston, 1902; member of the American Medical Association; school physician; visiting physician at the Lynn Hospital; died at his summer home in Nahant, September 30, aged 67, of coronary thrombosis.

J. H. Holiman, Dallas, Texas (licensed in Arkansas in 1903); served on the staff of the Pulaski County Hospital in Little Rock, Ark.; died September 15, aged 79, of heart disease.

Ross Holman Jones ✠ Coudersport, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; chairman of the Potter County Draft Board; served during World War I; on the staff of the Coudersport Hospital; died in the Olean (N. Y.) General Hospital October 23, aged 67, of chronic nephritis, uremia and arteriosclerosis.

Fred Warfield Lane ✠ Cambridge, Ohio; University of Pennsylvania Department of Medicine, Philadelphia, 1893; served during World War I; died in the Veterans Administration Facility, Chillicothe, October 11, aged 72, of arteriosclerosis and hypertension.

Lewis Wayne Law, Minneapolis; Harvard Medical School, Boston, 1943; interned at the Ancker Hospital in St. Paul; also a graduate in dentistry; began active duty as a lieutenant (jg) in the medical corps, U. S. Naval Reserve, on Oct. 10, 1944; released to inactive duty on Aug. 3, 1945; instantly killed by a bolt of lightning August 29, aged 29, while on the golf links in Lake Forest, Ill.

William Warner Meiners, Malverne, N. Y.; University of the City of New York Medical Department, 1891; member of the American Medical Association; for a time coroner in Long Island City; died October 20, aged 90, of chronic endocarditis, arteriosclerosis and coronary embolism.

Andrew John Muller ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1897; for many years on the staff of the Kensington Dispensary for Treatment of Tuberculosis; died October 31, aged 71, of carcinoma of the liver.

Michael E. O'Brien, Pittsburgh; University of Pennsylvania Department of Medicine, Philadelphia, 1896; member of the American Medical Association; died in St. Francis Hospital October 25, aged 75, of congestive failure.

Herbert Bittner Saylor, Des Moines; Rush Medical College, Chicago, 1908; died September 23, aged 68, of acute pyelonephritis and coronary arteriosclerosis.

Virgil Dural Selleck, Glens Falls, N. Y.; Albany Medical College, 1903; member of the American Medical Association; health officer; on the staff of the Glens Falls Hospital; died October 13, aged 68, of bronchopneumonia and carcinoma of the prostate.

Carl Schurz Tompkins, Randolph, N. Y.; University of Buffalo School of Medicine, 1901; member of the American Medical Association; served during World War I; formerly on the staffs of the City and Buffalo General hospitals in Buffalo, Batavia (N. Y.) Hospital and the Medina (N. Y.) Memorial Hospital; at one time on the faculty of his alma mater; died October 25, aged 73, of edema of the lungs and arteriosclerosis.

Paul Tradelius ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1904; specialist certified by the American Board of Ophthalmology; member of the Brooklyn Ophthalmological Society; consulting ophthalmologist at the Samaritan Hospital and assistant surgeon at the Brooklyn Eye and Ear Hospital; died in St. Mary's Hospital October 11, aged 71, of carcinoma.

John Alfred White II, Springfield, Pa.; Medico-Chirurgical College of Philadelphia, 1916; decorated with the Military Cross of England; received the Distinguished Service Cross and the Croix de Guerre for services during World War I; chief medical examiner of the Pennsylvania Railroad; died in Baltimore November 16, aged 51, of coronary thrombosis.

Samuel Wolf, Brooklyn; Fordham University School of Medicine, New York, 1919; member of the American Medical Association; died September 13, aged 62.

Charles Albert Yoder, Elm Creek, Neb.; Lincoln Medical College of Cotner University, 1902; served during World War I; died October 9, aged 70, of coronary thrombosis.

DIED WHILE IN MILITARY SERVICE

Morris I. Bierman ✠ Washington, D. C.; University of Minnesota Medical School, Minneapolis, 1920; born in Minneapolis Dec. 18, 1893; specialist certified by the American Board of Radiology, Inc.; served as assistant surgeon in the U. S. Public Health Service Reserve; on the staffs of the Emergency and Providence hospitals; began active duty as a lieutenant commander in the medical corps of the U. S. Naval Reserve in July 1942; on active duty in the Atlantic early in the war; for a short time stationed at the Naval Hospital at Bainbridge, Md.; for eighteen months had been on duty aboard an LST in the Pacific area; died Sept. 21, 1945, aged 51, of coronary thrombosis.

Joseph Harry Buckman, Albuquerque, N. M.; Northwestern University Medical School, Chicago, 1937; member of the American Medical Association; interned at the Evanston Hospital in Evanston, Ill.; began active duty as a lieutenant in the medical corps, U. S. Naval Reserve, on March 16, 1942; promoted to lieutenant commander; died in the U. S. Naval Hospital, Pensacola, Fla., Sept. 14, 1944, aged 38.

Daniel Joseph Hurley, Newton, Mass.; Harvard Medical School, Boston, 1909; born in Boston Nov. 16, 1881; formerly a member of the state board of registration in medicine; member of the Association of Military Surgeons of the United States; a captain in the medical corps of the U. S. Army at Camp Upton, L. I., and later chief of the surgical staff at Fort Bayard, N. M., during World War I; served on the staff of the Boston City Hospital; once surgeon for the Veterans Administration in Boston; began active duty as a lieutenant colonel in the U. S. Army (National Guard) on Jan. 16, 1941; executive officer of the 101st Regiment of the Twenty-Sixth (Yankee) Division until 1942, when he was named recruiting medical officer at Bangor, Maine; two years later became harbor defense surgeon at Portland, Maine, and since then had been on the staff of the Veterans Administration Facility in Newington, Conn.; died in the Lovell General Hospital, Fort Devens, October 15, aged 63, of coronary embolism.

John Kerr Macmillan Jr., Santa Monica, Calif.; College of Medical Evangelists, Los Angeles, 1938; member of the American Medical Association; diplomate of the National Board of Medical Examiners; interned at the Glendale Sanitarium and Hospital in Glendale; served a residency at the Santa Monica Hospital; began active duty as a first lieutenant in the medical corps, Army of the United States, on Feb. 28, 1944; promoted to captain on Aug. 1, 1945; died in Egypt Oct. 5, 1945, aged 37, of injuries received in an automobile accident.

Jewel Eugene Roberts, Salt Lake City; George Washington University School of Medicine, Washington, D. C., 1938; diplomate of the National Board of Medical Examiners; interned at the New York City Hospital in Welfare Island and the New York City Hospital in New York, where he served a residency; began active duty as a captain in the medical corps, Army of the United States, on July 8, 1942; died in the Station Hospital, Camp Kilmer, N. J., August 16, aged 33, of tsutsugamushi fever.

William Joseph Wagner ✠ Lieutenant (MC), U. S. Navy, New York; Jefferson Medical College of Philadelphia, 1939; interned at the Roosevelt Hospital; served an internship and residency at St. Vincent's Hospital; commissioned lieutenant (jg) in the medical corps of the U. S. Naval Reserve on June 16, 1942; later entered the medical corps of the regular U. S. Navy in the same rank; promoted to lieutenant; died near Sabine Pass, Texas, September 17, aged 32, of extreme multiple injuries received in an airplane accident.

Harvey Glenn Wible, Monessen, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1935; member of the American Medical Association; interned at the Homeopathic Medical and Surgical Hospital, Pittsburgh; formerly resident at the George F. Geisinger Memorial Hospital in Danville and the Shurly Hospital in Detroit; served on the staff of the Gemmill Hospital; began active duty as a first lieutenant in the medical corps, Army of the United States, on July 1, 1941; assigned to Station Hospital, Edgewood Arsenal, Maryland; later promoted to captain and major; killed in Hondo, Texas, Sept. 1, 1945, aged 35, in an airplane crash.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Dec. 29, 1945.

Public Health in India

The approach of self government for India has emphasized the appalling problem of the public health of that country of 420 million people. Western medical science has been able to touch only the fringe of the problem. India has only 42,000 doctors—one for every 10,000 people; India needs 300,000 doctors. There are only 5,000 trained midwives; 70,000 are necessary. The mass of the people still depend on indigenous medical systems which contribute little to the improvement of the national health, yet they claim and receive from several of the provincial governments privileges and grants grossly inadequate for scientific medicine. In most of India domiciliary treatment of the sick is difficult because of the miserable housing. The hospitals provide only 1 bed for every 3,000 persons. Tribute should be paid to the doctors, Indian as well as British, who have made many important advances in medicine and labored unceasingly to check epidemics and promote hygienic habits.

Indian vital statistics are imperfect, but their story is clear. The recorded death rate is 22 per thousand of population. The infant mortality is 162 per thousand live births. There is an average annual mortality of 145,000 from cholera, 70,000 from smallpox, 31,000 from plague, 290,000 from dysentery, 500,000 from tuberculosis and 3,667,000 from "fevers." The phenomenal increase of population renders the problem of public health more difficult. The Reconstruction Committee of the Viceroy's Council has recognized that a determined and coordinated attack on disease has long been necessary. Its success will depend on corresponding advances in the fields of education, housing and nutrition. A Health Survey and Development Committee, under the chairmanship of Sir Joseph Bhore, has been engaged on its immense task since the cold weather of 1943.

The Rehabilitation of the Medical Libraries of Europe

The Royal Society of Medicine has received from the Rockefeller Foundation $300,000 for setting up and maintaining for four years a Central Medical Library Bureau. The first objective of the bureau is the rehabilitation of medical libraries in the liberated countries, which have suffered so much during the war by German theft or devastation. The second and more permanent objective is the provision of rapid interchange of medical knowledge between individuals and institutions. At the present time the first objective is of paramount importance. Owing to the shortage of paper, means other than the use of printed paper must be considered. During the war the Royal Society of Medicine provided vital information for physicians in the forces overseas by microfilm. This experience will enable the society to perform a similar service in the restoration of medical libraries.

Soldiers Blinded by New Guinea Cherries

At the Liverpool Rotary Club Mr. C. D. Tovell, scientific adviser to the British forces in the Far East, stated that 27 soldiers, now back from fighting in New Guinea, were totally blind as a result of eating what looked like ordinary English cherries. The fruit was discovered at the end of 1942 and its lay name was "finger cherry." It looked and tasted like an English cherry. One or two of these cherries were eaten without ill effects, but soldiers who ate nine or ten became totally blind within a few hours. At present a means of restoring sight has not been found. As soon as the properties of the fruit were discovered, the authorities destroyed as many of the trees as possible.

British War Casualties

In the House of Commons the prime minister gave the total casualties of the armed forces of the British commonwealth and empire from Sept. 3, 1939 to Aug. 14, 1945 (excluding deaths from natural causes) as 1,246,025. This includes all men reported prisoners of war and in the armed forces of the United Kingdom, New Zealand, South Africa and the colonies, all men reported missing during the war. A final statement of casualties will be issued when the fate of those missing is determined and when all prisoners of war are repatriated.

PARIS

(From Our Regular Correspondent)

Jan. 9, 1946.

Doctors in France

A. Rosier, general secretary to the Office of University Statistics, has published in the *Médecin français* an article entitled "Do We Have Too Many Doctors?" For years this question has been unanswered. Since 1932 the Office of University Statistics has attempted to ascertain the optimum number of doctors and the localities needing them. Before the war it supplied information to young doctors regarding the distribution of doctors in France and provided a fund for loans to young doctors with inadequate means. During and shortly after the war the situation became disorganized. Numerous doctors were prisoners in Germany, others had left the devastated areas. Now the situation is becoming more normal again. There has been an appreciable increase in the number of first year students in the faculties of medicine, increasing from 2,071 in 1939 to 2,500 in 1944-1945. For the scholastic year 1945-1946 there has been a great influx of young people in the faculties of medicine because of the return of those deported, the demobilization and the abolition of racial laws. Notwithstanding this steady increase of students, the number of diplomas granted each year remains almost the same: 1,229 in 1900, 1,297 in 1932, 1,251 in 1944. However, 5 per cent of those who receive the diploma do not practice medicine. This year the number of graduates will increase, as in the period subsequent to the war of 1914-1918.

In spite of the constant number of students graduating each year there has been a constant increase in the number of practicing physicians from 15,907 in 1900 to about 27,000 in 1945. This increase is due to a yearly excess in the number of new doctors over those retiring or dying. This surplus was (on an average) about 219 doctors for the period 1910-1920 and 280 for 1920-1945. Rosier remarks that if these conditions continue France will have 3,000 more doctors in ten years. This increase is desirable because of the constant progress of medicine and the increased specialization of doctors, which gives them numerous openings.

In 1900 there was 1 doctor for every 2,445 inhabitants and there is now 1 doctor for 1,450; in several countries of Europe there is 1 doctor for 900 to 1,000 inhabitants. This distribution is very irregular in France. In Paris, Lyons, Toulouse and other important cities there is 1 doctor for 600 to 700 inhabitants; they are overworked and worn out. In numerous industrial centers or devastated areas there is 1 doctor for 3,000 to 4,000 inhabitants. In some places there is an entire absence of doctors. There is need for doctors in the French colonies and for medical inspectors in various institutions. The part time services of a doctor in every concern employing over 50 workmen is being considered as well as a full time doctor in every factory employing 2,000 to 2,500 workers.

Rosier concludes that a surplus of doctors does not exist but, on the contrary, there is need for more doctors and, above all, there is poor distribution of those available. He proposes that the state assist students with inadequate means, asking them, as compensation, to bind themselves to practice in less desirable districts for five or ten years.

Clitocybine, a New Antibacterial Substance

At the meeting of the Academy of Science held in September Prof. A. Charles Hollande presented a memorandum on a new antibacterial substance which he calls clitocybine. This product is extracted from Clitocybe gigantea, a large mushroom of the Agaricus family (Aspropaxillus). The author remarked that on alpine meadows of an altitude between 900 and 1,400 meters the grass around this mushroom does not develop, some dying without putrifying. On observing this he presumed that there was an active principle which inhibited the multiplication of microbes necessary for the putrefaction of vegetable tissues. This mushroom when cooked is edible, but when raw and dried it contains toxic substances. Clitocybine is soluble in water, chloroform, acetone and sulphuric ether; 0.005 cc. of a solution obtained after ether extraction and concentration in water prevents the development of the tubercle bacillus under certain specified conditions. To inhibit under the same conditions cultures of staphylococci, 0.025 cc. of the same solution is necessary. The inhibitory power of clitocybine is present also against Escherichia coli, Eberthella typhosa and Pseudomonas aeruginosa, against which penicillin is not effective. Repeated subcutaneous injections of tuberculous guinea pigs showed the massive lysis and disappearance of virulent tubercle bacilli.

Miscellaneous

At the reopening of the Paris University, 37 foreign scientists were elected doctors "honoris causa"; among those were Wesley C. Mitchell of Columbia University, W. T. Longcope of Baltimore, C. H. Best of Toronto, Horatio E. Smith of Columbia University, posthumously Edward K. Rand of Harvard University, Sir Alexander Fleming of London and Joffe of Moscow.

At its latest meeting the Academy of Medicine elected as foreign associated members E. D. Adrian of Cambridge, Sir Henry Dale of Picadilly, Sir Alexander Fleming of London, B. Houssay of Buenos Aires, George R. Minot of Boston, Theodore H. Morgan of San Francisco, L. A. Orbeli of Russia, Miguel Ozario de Almeida of Rio de Janeiro, Charles H. Best of Toronto and Ross G. Harrison of Washington.

ITALY

(From Our Regular Correspondent)

FLORENCE, Nov. 30, 1945.

Fractures of the Extremities

Dr. Pietre Franceschini, military surgeon serving at the front and in territorial hospitals near the front for the last four years, recently delivered a lecture to the Accademia Medico Fisica of Florence. He reported the results obtained in the therapy of fractures of the extremities, either simple (236 cases) or compound (1,256 cases). He obtained good results with either Bayer-Ombredanne's bandage or the classic posterior traction by means of Delbet's bandages in 125 cases of fracture of the clavicle. There were 17 cases of simple fracture of the shoulder. One soldier in this group had a fracture of the greater humeral tuberosity. The fractured fragment contained the greater tuberosity and a portion of the humeral head. Local anesthesia was applied, and the arm was put in abduction of 90 degrees and was immobilized for forty days in a Böhler splint, after which careful active mobilization was performed. Good results were obtained in other cases from abduction of the arm at 100 degrees with the elbow in extension.

There were 15 cases of noncomminuted diaphysial fractures of the femur. Immobilization with traction was carried out as soon as possible. Traction was obtained either by the Tillaux-Delbet technic with the Kirmisson pulley or by the Böhler technic with a nail in the tibia for transskeletal traction. The leg was placed in normal position on a double inclined plane. Immobilization with plaster cast was applied at the second stage of the operation. This method proved to be of great value. It produces gradual reduction of the fracture with a relatively small force of traction. Pain rapidly diminished. The clinical picture of gas embolism was never observed when this therapy was applied.

In the majority of cases the fractures were due to fragments of grenades or to shells from mortars and were more or less macerated. Primary definitive therapy in the fighting zones was never completed with a primary suture. Any of the following procedures were resorted to: capillary drainage, manual reduction of the fracture and application of a closed cast. Rational immobilization followed. Transskeletal traction was applied to the fracture in 18 cases for a period which varied from fifteen to forty days. Generally speaking, the wounded who were treated with this technic were able to be transported to hospitals far to the rear within ten or fifteen days. The mortality from compound fractures in the posts near the fighting zones was 2.5 per cent. In a group of 236 soldiers with war fractures treated in territorial hospitals, the great majority had been wounded one or two months before arriving at the hospital.

Medical Journals

The *Giornale di Medicina Militare*, which had been published for ninety-two years by the General Department of Military Sanitation, discontinued publication in June 1943. Now it has reappeared. Other medical journals which reappeared after the war are *Experimentale, Archivio di Biologia Normale e Pathologica, Ricerca Scientifica e Ricostruzione, Annali di Medicina Navale* and *Rivista Italiana di Igiene*. Dr. Alessandrini of the Pisa University was appointed editor of the *Rivista Italiana di Igiene* to succeed Dr. Filippe Neri, its previous editor, who died in the Instituto di Igiene of the Bologna University during an aerial attack.

Personal Items

Dr. Siro Fadda was recently appointed surgeon general in Italy. After his appointment he sent a message of salutation to all the members in the medical military service asking for their collaboration in reorganizing postwar military medicine and sanitation.

Colonel Dr. Guido Ferri was recently appointed chief of the School of Military Sanitation in Florence.

The Military Institute of Chemistry and Pharmacy, which was closed because of great destruction and pillage by the Germans, was recently reopened. Every effort is being made to reestablish the departments in which drugs and material for the army are prepared. Col. Giuseppe Scotti was appointed head of the institute.

Deaths

Dr. Giulio Chiarugi died on March 7, 1944. He was born in Siena on Jan. 28, 1859. He obtained the degree of Doctor of Medicine from the University of Turin in 1883. He was appointed regular teacher of anatomy on the Faculty of Medicine of the University of Siena in 1888 and held the same position on the Faculty of Medicine of the University of Florence for forty-one years. He published several books, among them a volume on general anatomy and a textbook on human anatomy which is in its sixth revised edition. He also wrote a textbook on embryology and published articles on the relation between the form of the cranium and the brain and on the structure of bone tissue and the histogenesis of muscular fibrous cells of the heart. Several of Dr. Chiarugi's pupils are now teachers of anatomy and related subjects in Italian universities.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANEIRO, Dec. 24, 1945.

Specific Rheumatic Fever

Dr. A. Penna de Azevedo, pathologist at the Oswaldo Cruz Institute, has reported a study on the incidence of rheumatic fever in Rio de Janeiro. Without an exact method of diagnosis, several criteria have been employed to ascertain the incidence of the disease. Rheumatic fever produces peculiar and characteristic lesions (Aschoff's nodules) generally associated with characteristic changes in the endocardium (rheumatic endocarditis) which permit better and surer criteria for the recognition of rheumatic fever than the clinical signs. The lesions can be recognized only by pathologic examination of the material, in the majority of instances taken during the performance of necropsies. Dr. Azevedo examined records of 6,700 necropsies accumulated in the files of the division of pathology of the Oswaldo Cruz Institute. By the examination of these records the author looked in some cases for the presence of the characteristic histologic lesion and in the majority of cases for changes in the myocardium, with the exception of those in which there was anatomic suspicion or certainty of syphilis. The incidence rate he found should be considered as the minimum incidence, because among other causes of error is the exclusion of the cases of bacterial endocarditis, which in about 75 per cent of the cases occurs in cardiac valves previously affected by rheumatism.

Of the total of 6,700 necropsies there were 589 cases of endocarditis, which was the cause of death of 8.82 per cent of the patients. According to etiology 417 cases of endocarditis were found to be rheumatic (6.22 per cent of the total necropsies), 106 cases syphilitic (1.58 per cent) and 66 cases malignant or bacterial (0.98 per cent). The 417 cases of rheumatic endocarditis (70.79 per cent of all cases of endocarditis) are distributed as 396 cases of valvular endocarditis (94.96 per cent) and 21 cases of mural endocarditis (5.04 per cent). Of the 417 cases of rheumatic endocarditis there were 247 in males (59.23 per cent) and 170 in females (40.77 per cent); there were 209 in white persons (50.12 per cent) and 208 in colored (49.88 per cent); there were 341 cases in Brazilian born persons (81.77 per cent) and 76 in foreign born (18.23 per cent). In the age distribution of 373 cases of rheumatic endocarditis it is significant to note that from ages 20-29 years there were 64 cases (17.16 per cent), 30-39 years 79 cases (21.18 per cent), 40-49 years 58 cases (15.55 per cent) and 50-59 years 57 cases (15.28 per cent), with 20 per cent of the cases occurring over the age of 60 years.

Courses and Lectures

Dr. Oswaldo Camargo, who recently returned from the United States, read a paper at the Hospital de Psiquiatria Infantil (a children's psychiatric hospital) presenting the modern features of psychiatric medical care in the United States.

Dr. Cyro de Rezende, associate professor of ophthalmology at the University of São Paulo, is now giving a special course of lectures and practical demonstrations on ocular neurology.

The University of São Paulo has announced two special courses in psychiatry to be given during the summer session (January and February) by Dr. Annibal Silveira, associate professor of psychiatry, and Drs. Darcy M. Uchoa and Paulo Lentino, physicians of the Juquery Psychiatric Hospital. Both these courses will be given at the Sanatorio Esperança.

Dr. Franklin de Moura Campos, professor of physiology at the University of São Paulo, recently read three papers in the auditorium of the medical department of the Food Relief Service of the Ministry of Labor in Rio de Janeiro. The first one was on the deficiency of certain special proteins, the second on special subjects of the physiopathology of nutrition and the third on the nutritive value of several foodstuffs peculiar to northern Brazil.

Brief Items

The second Pan American Congress of Ophthalmology, recently held in Montevideo, Uruguay, awarded a prize medal and an honor diploma to the administration of the city of Rio de Janeiro because of the distinguished services rendered by the Department of Hospitals in the field of ophthalmology. Dr. Joaquim Vidal, the representative of the department at the meeting, accepted the medal and the diploma.

The São Paulo chapter of the Brazilian Red Cross has opened a child welfare clinic in the city of São Paulo. The clinic is well organized and is provided with the best equipment.

The Rio de Janeiro Medical and Surgical Society recently commemorated its fifty-ninth anniversary. At a special meeting under the chairmanship of Dr. Joaquim Motta the society awarded several prize medals in commendation of the presentation of noteworthy papers on subjects of medicine and surgery. The prizes were awarded to Drs. A. Campos de Paz Filho, Americo Valerio and Aurelio Monteiro, who presented papers respectively on tubal sterility, vitamin A in the diet of air pilots and the Sloane technic in the treatment of feminine genital prolapse.

Personal

A telegram from Washington announced the arrival in that city of Dr. F. Godoy Moreira, orthopedic surgeon of São Paulo, who went to the United States as a guest of the State Department. Dr. Moreira will be present at the meeting of orthopedic surgeons in January 1946.

Dr. Charles Wagley, head of the Division of Health Education of the Special Service of Public Health, resigned this post and left for the United States to resume his work as professor at Columbia University. Dr. Wagley will continue to be associated with the SESP as a technical adviser.

Dr. J. Vieira Filho, who had been an active dermatologist at the Beneficencia Portugueza Hospital of this city, died at the age of 68. Although a Brazilian citizen, Dr. Vieira Filho graduated in medicine from the University of Porto, Portugal, and had worked for some time in Paris, France. He wrote several papers on subjects of dermatology and leprology.

Marriages

FRANCIS CURIE SKILLING, Key Field, Miss., to Leona Marie Mazzoni, Lieut., Nurse Corps, Army of the United States, at Drums, Pa., December 3.

ROBERT E. MCALPINE, Portsmouth, Va., to Miss Elizabeth Overton of Martinsville at Charlottesville, November 24.

ALLIE MCLEOD STANTON, Sylacauga, Ala., to Miss Margaret Elizabeth Spires of Edenton, N. C., December 14.

THOMAS JOSEPH SHEEHY JR., Augusta, Maine, to DR. ADELAIDE THERESE SCANLON of New York recently.

ROBERT NERCES ARMEN, Ithaca, N. Y., to Miss Eleanor Beatrice Baxter at Danville, Calif., November 4.

SUE HURST THOMPSON, Hudson, N. Y., to Mr. Edward Henry Gould of New York, November 3.

FRANK A. BENCHIK, East Chicago, Ind., to Miss Audrey Toussaint of St. Louis, November 19.

WALTER E. NAWROCKI, Cle Elum, Wash., to Miss Helen W. Zbikowski in Bristol, Conn., recently.

GLEA V. STANTON, Limestone, Tenn., to Miss Mildred Kathleen Cox in Newport recently.

CLIFF RATLIFF JR., Morven, N. C., to Miss Helen Jane Shaffer in Aberdeen, December 3.

JAMES LOUIE SMITH, Magnolia, Ark., to Miss Dede Dabbs of Gulfport, Miss., October 25.

CARYL POTTER JR. to Mrs. Patricia Blakeslee Davison, both of New York, October 11.

HENRY P. ROYSTER, Philadelphia, to Miss Ethel R. Fisher of Reedsville, Pa., recently.

EUGENE J. BOYD, Iowa City, to Miss Mabel Pullman of Centerville, October 13.

Correspondence

RELATION OF MENSTRUAL TOXIN TO ECLAMPSIA

To the Editor:—That you considered our investigations on menstrual toxin in relation to preeclampsia and eclampsia worthy of comment (THE JOURNAL, Nov. 17, 1945, p. 805) is gratifying. The title, "Menkin's Antinecrosin (Eclampsia Antitoxin)," is misleading. Dr. Menkin has demonstrated no antitoxic activity in antinecrosin serum. The fact that the serum of rabbits injected repeatedly with canine necrosin gives positive precipitin tests against this material (*Proc. Soc. Exper. Biol. & Med.* **56**:217 [June] 1944) is of no significance in this connection, since there is no preparation of necrosin free of other proteins. It was shown to Dr. Menkin in this laboratory that canine necrosin antiserum has as high a precipitin titer against normal dog serum as it has against canine necrosin. We had previously found (*Proc. Soc. Exper. Biol & Med.* **44**:100 [May] 1940; **55**:285 [April] 1944) that rats and rabbits could be made resistant to the toxicity of menstrual discharge and that transferable immunity was demonstrable. Such immune serum, however, could not be used in human beings because, our preparations of menstrual toxin being also mixtures of proteins, there would be the danger of reactions from antibodies to human proteins other than the toxic factor. Because we suspected that Menkin's pleural exudates and menstrual discharge contained the same toxic component, we had hopes that antiserum to necrosin of canine origin might have therapeutic possibilities against menstrual toxin without introducing this danger. Unfortunately, as pointed out in our publication (an item overlooked in the editorial), although menstrual toxin antiserum prolonged the survival time of rats given a minimal lethal dose of either menstrual toxin or canine necrosin, we were unable to get consistent results in attempts to demonstrate similar protective action with necrosin antiserum. The editorial wrongly suggests that it, as well as menstrual toxin antiserum, was effective against multilethal doses of toxin.

The principal value of necrosin antiserum proved to be that it provided a means, by cross precipitin tests, of establishing the fact that menstrual toxin and necrosin contained an identical protein and of demonstrating the presence of this same protein in the circulating blood of menstruating and toxemic women. Furthermore, these findings strengthened our hypothesis that the toxic protein might be a product of tissue damage in general and not just a "specific autolytic product of endometrial cells." We did not, as erroneously intimated in the editorial, demonstrate any higher precipitin titer in eclampsia than during menstruation, although we did find a greater concentration of fibrinolytic enzyme in preeclamptic and eclamptic serum.

The most promising lead from a therapeutic aspect lies in our finding of a protective substance against the "toxin" in the pseudoglobulin fractions of the human pleural exudates that we have tested and of the venous serum of menstruating or eclamptic patients. Such preparations consistently prolong the survival time of rats given a minimal lethal dose of menstrual toxin and often completely prevent death. They have the added advantage of being derived directly from human material and should therefore be comparatively safe to administer to human beings. We are at present attempting to prepare a concentrate of such material from which all elements of danger are removed.

O. WATKINS SMITH, PH.D.
GEORGE V. SMITH, M.D.,
Fearing Research Laboratory,
Free Hospital for Women,
Brookline, Mass.

RECURRENT HEADACHE IN MALARIA

To the Editor:—In the January 5 issue of THE JOURNAL Comdr. Frederick A. Butler (MC), U.S.N., takes issue with some of my statements in the report on Recurrent Headache Resultant from Malarial (THE JOURNAL, Oct. 27, 1945, p. 612). There was nothing in my report which implied any danger or likelihood of a significant outbreak or increase of malaria in the United States. It simply stressed that quiescent and recurrent cases of malaria will be encountered more frequently as more men who were stationed during part of their duty on malarious islands return from the Pacific area. This is to be expected, for we know that neither atabrine nor quinine cures the disease; they only suppress it.

We know further that recurrent attacks of malaria are often precipitated by acute infections, exhaustion, malnutrition and alcoholism. Recurrent headache is usually the first and most distressing symptom to usher in an attack of malaria.

The main point of my report was only to emphasize that malaria is a "great imitator" and should be included with greater frequency in the differential diagnosis of recurrent headache.

In our experience on Guam we found the provocative measure of the administration of 15 grains (1 Gm.) of quinine or ephedrine 2 minums (0.12 cc.) subcutaneously surprisingly helpful in establishing the diagnosis of malaria when smears were negative previously. It is not assumed that those who did not respond to the provocative test did not have malaria, no more than it can be assumed that a negative blood Wassermann reaction rules out syphilis.

ABRAHAM KAPLAN, Captain (MC), U.S.N.R.

Bureau of Investigation

SOME MISCELLANEOUS MEDICAL FRAUDS

A Variety of Schemes Debarred from the Mails

Fraud orders issued by the Post Office Department have frequently been the subject of extensive articles by the Bureau of Investigation in these pages of THE JOURNAL. Following are brief abstracts of some fraud orders not dealt with previously:

Salvar Medicine Company.—This St. Louis concern is said to have been started in June 1906 by a Charles E. Gallagher, a civil engineer, who previously had run a "patent medicine" outfit in Kansas City, Mo., selling a nostrum called "Alkano." In 1908, it is reported, the St. Louis firm took the name "Salvar Medicine Company of Arizona" and established agencies in various cities. Around 1921, it appears, an Edward L. Eggers joined the business as "medical director," and became the proprietor in 1923. According to the records, he was licensed to practice medicine in Missouri in 1900 and was said to have claimed graduation from the St. Louis College of Physicians and Surgeons. This institution was involved in the "diploma mill" scandal of 1923 and 1924, and its charter was revoked in 1927. A John E. Eggers, said to be a brother of Edward L. Eggers, is reported to run the Newell Pharmacal Company of St. Louis and Clayton, Mo., which puts out another nostrum, "Tobacco Redeemer." Through the mails the Salvar concern, sometimes known as the Gallagher Medicine Company, sold its "Salvar" and, for a time, boldly claimed: "Salvar Remedy will cure syphilis perfectly, positively and permanently in any stage of the disease, even though the bones themselves are rotten." It was also promoted for rheumatism, chronic constipation, catarrh, malaria, diseases of the liver, kidneys and bladder, female disorders, tuberculosis, heart ailments, and some other things. Finally the Post Office Department caught up with this quackery and, after due investigation, notified the promoters to show cause why a fraud order should not be issued against them. In reply, Edward L. Eggers denied having made "false or fraudulent representations or promises," and declared that he had discontinued the sale of Salvar and the practice of medicine by mail, had "closed up" his business and accordingly urged that no fraud order be issued against him. Neither he nor anyone representing him, however, attended the hearing of the case, held in Washington on August 9, 1943. At that time a government chemist testified that his analysis of the Salvar specimen purchased from the company by mail showed it to be a solution consisting of water and 30.2 per cent of alcohol, the rest being essentially berberine, acid chloroform extract, cascara, tannin, invert sugar, podophyllum, guaiac, echinacea (or bloodroot, or both), iodine, spearmint, sarsaparilla, possibly eucalyptus, and traces of mineral matter. An expert medical witness testified for the government that he was familiar with all these ingredients and their effects; that the chief action of the mixture would be laxative because of the podophyllum and cascara present, and that the only other drug worth mentioning was iodine, and the amount present was insufficient to constitute a therapeutic dose. He further pointed out that the diet and hygiene suggestions sent out with the

nostrum were irrelevant, and showed the worthlessness of Salvar in syphilis and the other disorders mentioned. A fraud order accordingly was issued on Nov. 23, 1943, against the Salvar Medicine Company and Edward L. Eggers.

Natural Health Institute.—This enterprise was conducted at Rocky Mount, N. C., by a "Dr." J. Lewis Clinton, a chiropractor and author of so-called health writings. Further, he published two booklets, "Radiant Health Through Normal Elimination" (27 pages) and "Energy Unlimited" (58 pages). These were advertised by means of a circular entitled "Your Health!" The Post Office Department charged that these booklets were misleading and that the sale of them through the mails constituted a fraud on the public. Clinton, however, was given opportunity to appear at a hearing and show cause why a fraud order should not be issued debarring his business from the mails. A Senior Medical Officer for the Food and Drug Administration who appeared as a witness for the government at the hearing testified as to the factors causing constipation, which condition was the subject chiefly dealt with in the first-named booklet. He pointed out that Clinton's pre-sale allegations that his advice would enable patrons to "free" themselves from enemas, laxatives and other "adjuncts" contrasted with his suggestion in the book that if the methods he advocated (going to stool preferably after breakfast and massaging the lower part of one's abdomen in a certain way) failed to work, a mild laxative should be employed or a soapsuds enema used. It was further pointed out that though his pre-sale representation was that "no dieting" and "no exercises" would be required, both dietary suggestions and exercises are included in his book. The witness further showed that different cases of constipation require varying methods of treatment. As to the book "Energy Unlimited," the leaflet advertising it called it "one of the biggest surprises in the health book field, and utterly unlike anything you have ever read," in which "Dr. Clinton presents conclusive evidence to show that chronic fatigue, nervousness, sleeplessness and associated symptoms of nerve exhaustion are not due so much to a lack of energy itself, but to a lack of proper transmission and expression of energy . . . to tensions and 'short-circuits' which squeeze the nerves and decrease the flow of energy. . . ." The government's expert medical witness testified that the symptoms mentioned above are those of practically all diseases; that Clinton's theory of nerve pressure was a distorted one, and that the diet prescribed in his book for the purpose of forming an alkaline balance in the system is diametrically opposed to that of taking exercise (which Clinton also advocated), since exercise tends to produce an acid condition as opposed to the alkaline-forming diet. Although Clinton did not appear at the hearing, he filed an answer to the foregoing testimony, in which, however, he offered no evidence of the efficacy of the measures recommended in the two booklets mentioned. He did deny any intention to defraud. Nevertheless, the Post Office Department held that the charges against him were entirely sustained by the evidence, and recommended a fraud order debarring him from the mails. This was issued August 14, 1944, against the Natural Health Institute, "Your Health!", "Dr." J. Lewis Clinton, editor and publisher, and W. M. Vandiford, publications department, as well as their officers and agents.

Mary Ries Melendy Ostine Company.—This concern, whose address was Stillwater, Minn., apparently was an outgrowth of the business that was started years ago in Chicago by Mary Ries Melendy, M.D., a homeopathic physician who died in 1927. Some time thereafter the business seems to have been transferred to Stillwater, Minn., by her son, Charles E. Ries. After an investigation, the Post Office Department notified the company and Charles E. Ries, Distributor, to show cause why a fraud order should not be issued against them. Ries did not appear at the hearing of the case held in Washington, but filed a written answer in which he claimed to be a registered pharmacist but for seventeen years engaged in selling through the mails certain homeopathic remedies made in accordance with prescriptions of his mother, who had sold them to her patients for about fifty years. A chemist and a microanalyst of the Food and Drug Administration testified for the government at the hearing, showing that "Dr. Melendy's Brain and Nerve Food" consisted essentially of 98.6 per cent of milk sugar, with traces of calcium, iron, sulfate and phosphate; that "Balm Palmetto Female Tonic" was 99.5 per cent milk sugar, and the remainder moisture and traces of iron, calcium, phosphate, possibly magnesium and minute traces of other minerals. The "Balm Palmetto Capsules" were reported to consist of some greasy material with an odor of cocoa butter, in which was a small amount of plant material, including hydrastis, together with ½ grain of iodine per capsule, combined probably as a sodium salt, and perhaps some saw palmetto, and the "Balm Palmetto Cerate" was found to be a yellowish ointment consisting of 98.2 per cent of petrolatum and 1.8 per cent of moisture. These witnesses further testified that "No. 1 Tokoine" was a mixture of coarsely ground herbs, chiefly coltsfoot leaves, with much smaller amounts of catnip herb, black snakeroot and an unidentified leaf, and that "No. 2 Tokoine" consisted of very finely ground lobelia herb. The Tokoine combination was represented to eliminate pain in childbirth. "Tri-Cura," for rectal disorders, was shown to consist of capsules apparently containing cocoa butter, a small amount of plant material, including hydrastis, and a trace of iodine. "Ostine No. 1," which a pamphlet declared was a "cure" for various disorders in children, was, the witnesses reported, a white powder consisting essentially of 98.4 per cent of milk sugar, with traces of calcium and insoluble material, probably silica, whereas "Ostine No. 2" for "developing" growing children, was found on analysis to be a white powder containing about 98.7 per cent of milk sugar, with traces of calcium, iron and phosphate. An expert medical witness for the government testified as to the worthlessness of these various nostrums in the conditions for which they were advertised, and the business was declared by the Post Office Department to be a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises. Accordingly, a fraud order was issued on Oct. 23, 1944, against the Mary Ries Melendy Ostine Company, Charles E. Ries, Distributor, and Charles E. Ries, the individual.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Osteopaths: Rights Under E. M. I. C. Program.—An act of Congress, chapter 221, Public Law 135, known as "Labor-Federal Security Appropriations Act, 1944" under the subtitle "Maternal and Child Welfare" provided for the grant of money to states for emergency maternity and infant care for the wives and infants of certain enlisted men and aviation cadets in the armed forces of the United States. The use of federal funds received by any state was made subject to the following restriction:

> . . . Provided, That no part of any appropriation contained in this title shall be used to promulgate or carry out any instruction, order or regulation relating to the care of obstetrical cases which discriminates between persons licensed under state law to practice obstetrics: Provided, further, That the foregoing proviso shall not be so construed as to prevent any patient from having the services of any practitioner of her own choice, paid for out of this fund, so long as state laws are complied with.

In both Wisconsin and Texas the plans submitted by the state board of health and subsequently approved by the Children's Bureau eliminated osteopaths from receiving payment for services out of funds made available for the E. M. I. C. program by requiring that the physicians furnishing the services be graduates of a medical school approved by the Council on Medical Education and Hospitals of the American Medical Association. In Wisconsin the osteopaths protested by filing an action asking for a declaratory judgment as to the validity of the state plan. From an order overruling the defendants' demurrer, the state board of health appealed to the Supreme Court of Wisconsin. In Texas, a few months later, the osteopaths filed suit for an injunction to restrain the state board of health from operating under its plan until it had been so amended as to permit osteopaths to participate. From a judgment for the plaintiffs, the defendant appealed to the court of civil appeals, Austin, Texas.

In Wisconsin the state board of health demurred on the ground that the complaint did not state a proper case for declaratory relief. The Supreme Court said that the allegations were

> solely concerned with the proper distribution of federal funds by a federal administrative board, through the Wisconsin state board of health acting as its agent. The several appropriations made by Congress to carry out the E. M. I. C. program were all made to the United States Department of Labor, Children's Bureau, which bureau allots the funds to the several states to carry out the program according to plans approved by the federal bureau. That puts this controversy out of our reach. No facts are alleged in the complaint to the effect that any osteopath has been deprived of the right to practice obstetrics or that any such action has been threatened. Neither is any declaration demanded along this direction. The pleadings, therefore, state no cause of action for declaratory relief on this point. . . .

Accordingly the judgment in favor of the osteopaths was reversed and an order entered sustaining the defendant's demurrer.

In Texas the state board of health contended that the state courts lost jurisdiction of this case because of the rule that

> In the absence of Congressional sanction, state courts cannot entertain suits against the United States or its agencies, including corporations created by the national government, and are without jurisdiction to control or restrain the official conduct of federal officers or agents. federal courts having exclusive jurisdiction over such suits. (21 C. J. S. 796.)

This appropriation act, said the court of appeals of Texas, does not sanction or authorize state courts to entertain suits with respect to any matter arising thereunder. Under such appropriation act the members of the state board of health are not acting as state officials but merely as the agency of the federal government through which the appropriation is to be expended. The act does not authorize the members of the state board of health to receive or administer any portion of the funds appropriated and allotted to Texas, the court continued, except under a plan approved by the chief of the Children's Bureau. The record in this case showed that the Children's Bureau in fact outlined the plan for the administration of the fund allotted to Texas and approved such plan as required by the act. Neither the act nor any Texas statutes undertake to authorize the mem-

bers of the state board of health to act in any manner except as an agency of the federal government in administering the federal fund appropriated by the Congress to aid in the care of wives and infants of certain enlisted men. The court then quoted with approval the statement quoted from the Wisconsin decision and in reference to such quotation said that

> The foregoing quotation from the Hecker case overruled the contention of appellees that the Congress, under the appropriation act in question, leaves the development and setting up of the plan for the disbursement of the funds wholly to the state health agencies. The Act provides that the state health agencies must adopt rules for the distribution of the funds, and who may participate in care of the wives and infants of soldiers and aviators, but expressly provides that such rules and plans must be approved by the Children's Bureau at Washington; and, as was said in the Hecker case, "it was the approval of the plan by the federal bureau that gave the E. M. I. C. program its vitality."

Accordingly the judgment in favor of the osteopaths was reversed and the injunction dissolved.—*Hecker v. Gunderson, 15 N. W. (2d) 788 (Wis., 1944); State Board of Health v. Wilson, 188 S. W. (2d) 999 (Texas, 1945).*

Constitutionality of Illinois Medical Practice Act Sustained.—An information in four counts charging violation of the medical practice act was filed against the defendant. From a judgment of guilty he appealed to the Supreme Court of Illinois.

The only errors assigned related to the constitutionality of the medical practice act, the defendant's first argument being that the medical practice act violates section 13 of article IV of the constitution of the state of Illinois in that it embraces more than one subject. The title of the act is "An Act to revise the law in relation to the practice of the treatment of human ailments for the better protection of the public health and to prescribe penalties for the violation thereof." It is urged that the sections of the act which regulate the practice of midwifery deal with a subject other than the "treatment of human ailments for the better protection of the public health." It is universally recognized, said the Supreme Court, that insanitary and improper methods employed by those engaged in the practice of midwifery are often followed with serious results to the health of the mother and child. The regulations provided in the act are for the protection of health and within the title of the act. The constitutional question pleaded does not furnish the semblance of a debatable issue.

The defendant next argued that the medical practice act violates the due process clause of the constitution in that it forbids the doing of certain things which are not the subject of regulation. The defendant referred to section 2 of the act providing that no person shall engage in the practice of medicine or midwifery without being licensed as provided by statute. Emphasis is placed on the designation "no person" and it is urged that such an all inclusive term prohibits any one not licensed from ministering simple home remedies to minor ailments. Section 2, said the court, must be considered in the light of the other sections and the purposes sought to be accomplished by the whole enactment. When so considered the contention made appears frivolous. The defendant was convicted for a violation of section 24, which specifies the elements of the offense, a part of which is a holding out to the public as being engaged in diagnosis or treatment of ailments of human beings, suggesting, recommending or prescribing treatment for relief of ailments, all with the intention of receiving directly or indirectly a fee or reward therefor. It is clear, the court concluded, that the act is not subject to the criticism directed against it.

Finally the defendant argued that the act is vague and meaningless and directs an administrative board to do certain things without furnishing a standard for its guidance. The court's attention was directed to that part of section 3 which provides that no person, subject to certain exceptions, shall hereafter receive a license unless he shall pass an examination, etc., satisfactory to the department, and to section 4, which requires each applicant for license to submit certain proof under oath "satisfactorily to the Department." The court said that not only had the validity of the medical practice act been sustained against attack from various angles in prior decisions but objections similar to those made by defendant had been decided adversely to his contention in a number of prior cases (citing them). Accordingly the Supreme Court affirmed the judgment of guilty. —*People v. Zimmerman, 63 N. E. (2d) 850 (Ill., 1945).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Board in Specialties were published in THE JOURNAL, Feb. 2, page 305.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Mar. 19-21. Sec. Dr. B. F. Austin, 519 Dexter Ave., Montgomery 4.

ALASKA: Juneau, March 5. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA: * *Examination.* Phoenix, April 2-3. *Endorsement.* Phoenix, April 6. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Medical.* Little Rock, June 6-7. Sec., Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Eclectic.* Little Rock, June 6. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* Los Angeles, March 11-14. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

COLORADO: Denver, April 2-5. Final date for filing application is March 18. Sec., Dr. J. B. Davis, 831 Republic Bldg., Denver.

CONNECTICUT: * *Medical. Examination.* New Haven, March 12-13. *Endorsement.* New Haven, March 26. Sec. to the Board, Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic.* Derby, March 12-13. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, April 9. *Reciprocity.* Dover, April 16. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * *Reciprocity.* Washington, March 11. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington 1.

FLORIDA: * Jacksonville, June 24-25. Sec., Dr. Harold D. Van Schaik, 2736 S.W. Seventh Ave., Miami 36.

GEORGIA: Atlanta and Augusta, March 27-28. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

IDAHO: Boise, July 9. Dir., Bureau of Occupational Licenses, Miss Agnes Barnhart, 355 State Capitol Bldg., Boise.

ILLINOIS: *Examination.* Chicago, April 2-3. *Reciprocity.* Chicago, April 4. Supt. of Registration, Department of Registration & Education, Mr. Philip Harman, Springfield.

INDIANA: Indianapolis, April 25-27. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis 4.

IOWA: * Iowa City, March 25-27. Dir., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines 19.

KANSAS: Kansas City, March 12-13. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. Seventh St., Kansas City 10.

KENTUCKY: Louisville, March 25-27. Sec., State Board of Health, Dr. Philip E. Blackerby, 620 S. Third St., Louisville 2.

MAINE: Portland, March 12-13. Sec., Board of Registration of Medicine, Dr. A. P. Leighton, 192 State St., Portland.

MASSACHUSETTS: Boston, March 12-15. Sec., Board of Registration in Medicine, Dr. H. Q. Gallupe, 413-F State House, Boston.

MICHIGAN: * Detroit, March 26-28. Sec., Board of Registration in Medicine. Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MISSISSIPPI: June. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson 113.

MISSOURI: *Examination.* St. Louis, Feb. 25-27. Sec., State Board of Health, Dr. R. M. James, State Capitol Bldg., Jefferson City.

MONTANA: Helena, April 1-3. Sec., Dr. O. G. Klein, First National Bank Bldg., Helena.

NEW JERSEY: Trenton, June 18-19. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 8-9. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NEW YORK: Jan. 28-31. Sec., Dr. Jacob L. Lochner, Education Bldg., Albany.

NORTH CAROLINA: Raleigh, March 25-28. Act. Sec., Mrs. Louise J. McNeely, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: Grand Forks, July 2-3. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Examination.* Columbus, March 19-22. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, March 23. Sec., Dr. J. D. Osborn Jr., Frederick.

PENNSYLVANIA: Philadelphia and Pittsburgh, April. Act. Sec., Bureau of Professional Licensing, Department of Public Instruction, Mrs. M. G. Steiner, 351 Education Building, Harrisburg.

RHODE ISLAND: Providence, April 4-5. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, Feb. 24-26. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Pierre, July 16-17. Sec., Medical Licensure, State Board of Health, Dr. Gilbert Cottam, Capitol Bldg., Pierre.

TENNESSEE: * Memphis and Nashville, March 27-29. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis 3.

TEXAS: Austin, March 27-29. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

VERMONT: Burlington, March or April. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: * Richmond, March 25-28. Sec., Dr. J. W. Preston, 803 Medical Arts Bldg., Roanoke.

WYOMING: Cheyenne, Feb. 4. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: Feb. 9. Address State Board of Healing Arts, 250 Church St., New Haven 10.

FLORIDA: Gainesville, June 4. Final date for filing application is May 20. Sec. Dr. J. F. Conn, John B. Stetson University, DeLand.

OREGON: Portland, March 2. Sec., Board of Higher Education, Mr. C. D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: Providence, Feb. 13. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1936 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Psychiatry, New York

102:145-288 (Sept.) 1945. **Partial Index**

Prolonged Posttraumatic Syndromes Following Head Injury. J. Ruesch and K. M. Bowman.—p. 145.

Conjectured Correlation Between Depressions of Manic Depressive and Involutional Melancholic Types and Ethnic Elements in Present Day Population of Britain. R. Gibson.—p. 164.

What Happens to Patients Who Are Hospitalized for First Time When over Sixty-Five Years of Age. O. Camargo and G. H. Preston.—p. 168.

Memory Function: I. Factorial Study of Fifteen Clinical Tests. H. J. Eysenck and H. Halstead.—p. 174.

Clinical Note on Significance of Validity Score (F) in Minnesota Multiphasic Personality Inventory. A. T. Kazan and I. M. Sheinberg.—p. 181.

Bilateral Internal Jugular Blood: Comparison of A-V Differences, Oxygen-Dextrose Ratios and Respiratory Quotients. Erna L. Gibbs, W. G. Lennox and F. A. Gibbs.—p. 184.

Presenile Dementia (Alzheimer's Disease): Its Pathogenesis and Classification, with 2 Case Reports. K. Stern and G. E. Reed.—p. 191.

Saint Vincent de Paul—Saint Louise de Marillac and Their Daughters: Their Care of the Insane. Mary E. Walsh.—p. 198.

Marihuana, an Intoxicant. H. S. Gaskill.—p. 202.

Neuropsychiatric Problems at an Aleutian Post. G. C. Burns.—p. 205.

Statistical Study of 100 Neuropsychiatric Casualties from Normandy Campaign, with Control Material. W. Needles.—p. 214.

Problem of Severe Psychoneurotic in Army Air Forces. J. W. Bick Jr.—p. 222.

*Sociologic Factors in Patients in Army Neurosis Center and Their Relation to Disciplinary Actions. P. V. Lemkau and F. E. Kent.—p. 231.

Two Different Types of Posttraumatic Neuroses. A. Adler.—p. 237.

Incidence of Nail Biting Among Adults. L. A. Pennington.—p. 241.

Fraternity in Combat. D. E. Johnson and J. T. Thickstun.—p. 245.

Young Delinquent. Doris Chaplin.—p. 257.

Psychoses Among Women Government Workers in Wartime. H. Stevens.—p. 260.

Sociologic Factors in Neurosis.—Lemkau and Kent review 968 cases admitted to an army neurosis center. They found that normal homes produce a significantly smaller proportion of military delinquents than broken homes. While there is an apparent tendency for the homes with inadequate finances to produce a larger proportion of military delinquents, this is statistically not significant. Patients with an urban background are somewhat more likely to be military delinquents than those of rural background. Military delinquency is not significantly related to marital status in this group of patients. Men who have held but one job before entering the service are less likely to become military delinquents than men who have badly disorganized work histories.

American Review of Tuberculosis, New York

52:269-354 (Oct.) 1945

*Streptomycin in Experimental Tuberculosis. W. H. Feldman, H. C. Hinshaw and F. C. Mann.—p. 269.

*Streptothricin in Experimental Tuberculosis. W. H. Feldman and H. C. Hinshaw.—p. 299.

Chemotherapy of Sulfones and Sulfonamides in Experimental Tuberculosis. M. I. Smith and W. T. McClosky.—p. 304.

Anatomic Studies on Human Tuberculosis: XIX. Protracted Primary Tuberculosis in the Adult, with Some Observations on "Lymphoglandular-Endogenous Reinfection (Ghon)." K. Terplan.—p. 312.

Eosinophilia in Silicosis. W. J. Habeeb.—p. 337.

Tuberculosis of Tongue. L. L. Titche.—p. 342.

Founders of National Tuberculosis Association. R. G. Paterson.—p. 345.

Streptomycin in Experimental Tuberculosis.—Feldman and his co-workers report three experiments on guinea pigs, the first two being of short duration, the third extending over a 215 day period. In the latter, guinea pigs were inoculated with Mycobacterium tuberculosis forty-eight days before treatment with streptomycin was started. The animals received 6,000 units of streptomycin daily divided into four equal doses. The treated group consisted of 25 guinea pigs, while the group of untreated controls totaled 24 animals. When the experiment was terminated after 166 days of treatment, 17 of the untreated animals had died, compared to 2 of the group that had received streptomycin. Nearly all of the untreated controls showed at necropsy severe, widely disseminated tuberculosis while the tuberculous disease among the animals that had been treated was minimal. Thirteen of the treated animals had no tuberculosis grossly or microscopically. Nine of the treated animals living when the experiment was terminated gave a negative reaction to tuberculin. The authors conclude that streptomycin was effective in resolving or suppressing established experimental tuberculous infection in guinea pigs. The streptomycin preparations used had a low toxicity for guinea pigs in doses of 6,000 units per day and were tolerated without recognizable deleterious effects for a prolonged period. Although capable of combating or preventing anatomic changes due to Mycobacterium tuberculosis, streptomycin in most instances exerted a suppressive rather than a sterilizing effect on the infective agent. In some instances successful treatment with streptomycin resulted in the reversal of a positive sensitivity to tuberculin. Larger doses and more frequent administration of streptomycin might have enhanced the bacteriostatic effects. The striking effects of streptomycin in reversing a potentially lethal tuberculosis in the highly susceptible guinea pig and the low toxicity and corresponding safety of purified streptomycin are prerequisites of a drug worthy of clinical trial.

Streptothricin in Experimental Tuberculosis.—Feldman and Hinshaw tested streptothricin in experimental tuberculosis in guinea pigs. The streptothricin available and in the dose used was poorly tolerated by large, previously vigorous guinea pigs. Seven of the 10 guinea pigs treated with streptothricin died during sixty-one days of observation. Unlike streptomycin, which has a high therapeutic potential in tuberculosis of guinea pigs, streptothricin proved devoid of deterrent qualities that would suggest antituberculosis effects.

Archives of Internal Medicine, Chicago

76:131-188 (Sept.) 1945

*Etiology and Pathogenesis of Rheumatic Fever. L. A. Rantz, P. J. Boisvert and W. W. Spink.—p. 131.

Characteristic Vascular Pattern in Patients with Rheumatoid Arthritis. M. Naide, Ann Sayen and B. I. Comroe.—p. 139.

Gallbladder Dye (Iodophthalein Sodium): Effect of Intravenous Injections on Coronary Flow, Blood Pressure and Blood Coagulation. F. E. Lawson.—p. 143.

Changes in the Central Nervous System Associated with Encephalitis Complicating Pneumonia: I. Clinical Study. A. B. Baker and H. H. Noran.—p. 146.

*Putrid Pulmonary Abscess Without Foul Sputum (Shut-Off Pulmonary Abscess). D. Stats and H. Neuhof.—p. 154.

Sulfonamide Compounds and Penicillin: Effect of Combined Therapy on Experimental Infections in Mice. E. H. Sultan, D. W. Jenkins and W. C. Cutting.—p. 161.

Tularemic Meningitis: Review of Literature and Report of Case, with Postmortem Observations. B. M. Stuart and R. L. Pullen.—p. 163.

Intravenous Injection of Acacia: Clinical and Physiologic Effects on Patients with Nephrotic Edema. J. B. Johnson and L. H. Newman.—p. 167.

Recurrent Meningoencephalitis Due to Virus of Lymphogranuloma Venereum. D. W. Scott Jr.—p. 174.

Etiology and Pathogenesis of Rheumatic Fever.—Patients discovered to have a hemolytic streptococcus infection in army camps were transferred to special wards and were studied by means of a variety of laboratory procedures. Cultures were made repeatedly from the nose and throat, and the isolated hemolytic streptococci were classified serologically by the precipitin technics of Lancefield. Serial white blood cell counts, erythrocyte sedimentation rates (Westergren) and electrocardiograms were obtained. Each patient was studied for not less than three weeks and frequently for a longer period. During the period of intensive study, from Jan. 1 to April 15, 1944, approximately 1,500 patients were observed. As the basis for further investigation, Rantz and his associates point out (1) that rheumatic fever is invariably induced by infection with group A hemolytic streptococci, (2) that this syndrome is but a part of the whole complex involved in the poststreptococcic state, (3) that these clinical manifestations are the result of altered sensitivity of the tissues to products of the hemolytic

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streptococcus and (4) that repeated infection with different types of hemolytic streptococci may be necessary for the development of these disorders. If this working hypothesis is acceptable, it would appear (1) that sensitivity of the tissues must occur to some fraction or product of the hemolytic streptococcus and (2) that this fraction or product must be common to all types of group A streptococci. It would seem desirable to obtain these substances in highly purified form and to determine whether they have induced the formation of circulating antibodies and whether the tissues of rheumatic persons are sensitive to them. Such an investigation might lead to technics which would permit the determination of dangerous streptococcus hypersensitivity and to possible preventive or therapeutic measures.

Putrid Pulmonary Abscess Without Foul Sputum.—Stats and Neuhof report instances of acute putrid pulmonary abscess without foul sputum. They have termed this variety "shut-off abscess" on the assumption that the bronchus communicating with the abscess is occluded as a result of an inflammatory reaction and cannot drain the contents of the abscess. The shut-off pulmonary abscess has a tendency to invade the pleura. The presence of such an abscess should be considered when (1) a cause for a putrid pulmonary abscess exists (or, in the absence of a cause, dental hygiene is poor), (2) thoracic pain is severe, prolonged or recurrent, (3) cough and expectoration are minimal or absent and (4) x-ray examination reveals persistent pulmonary infiltration with or without pleural effusion. There are grave dangers inherent in a too long delayed diagnosis. If the possibility of this lesion is borne in mind, a correct diagnosis can be made. The excellent results achieved by adequate operations on the pulmonary abscess and on the complicating empyema that is often present provide an additional incentive to establishing the diagnosis of shut-off putrid pulmonary abscess.

Archives of Neurology and Psychiatry, Chicago

54:163-230 (Sept.) 1945

Studies on Cerebral Edema: I. Reaction of Brain to Air Exposure; Pathologic Changes. M. Prados, B. Strowger and W. H. Feindel.—p. 163.
Tremors of Combat Neuroses: Comparison with Tremors of Paralysis Agitans, Delirium Tremens and the Psychoneuroses of Civilian Life; Electromyographic Studies. M. A. B. Brazier.—p. 175.
*Arteriovenous Aneurysm of Great Cerebral Vein and Arteries of Circle of Willis: Formation by Junction of the Great Cerebral Vein and the Straight Sinus and by the Choroidal Arteries and Anomalous Branches of the Posterior Cerebral Arteries. B. J. Alpers and F. M. Forster.—p. 181.
Incidence of Advanced Maternal Age in Mothers of 1,000 State Hospital Patients. H. Barry Jr.—p. 186.
Ménière's Syndrome: Comparison of Results of Medical and Surgical Treatment. M. Atkinson.—p. 192.
Electroencephalographic Localization and Differentiation of Lesions of Frontal Lobes: Pathologic Confirmation. C. L. Yeager and S. Luse.—p. 197.
Schizophrenic Reaction Syndrome in Course of Acute Demyelination of Central Nervous System: Clinicopathologic Report of a Case, with Brief Review of Literature. L. Roizin, J. D. Moriarty and A. A. Weil.—p. 202.
Visual Retention Test for Clinical Use. A. L. Benton.—p. 212.

Arteriovenous Aneurysm of Great Cerebral Vein and of Circle of Willis.—The patient observed by Alpers and Forster was a youth aged 18 who was hospitalized because of headaches from which he had suffered since the age of 6. They were frontal, occurred once or twice a week and became more severe two months before entrance into the hospital. In the last month the headaches were accompanied by dizziness, characterized by movement of objects in the environment. The patient was somewhat euphoric, highly distractible and rather flippant. His reactions were slow; the intelligence quotient was 64 by the Stanford-Binet test. Because of the history of persistent headache and the evidence of calcification in the roentgenogram, a diagnosis of brain tumor was made. Ventriculographic examination revealed greatly dilated ventricles. The right lateral ventricle was opened. At the glomus of the choroid plexus a large, tortuous mass of arteries and veins was found which ran toward the base of the skull and connected with the large vessels, supplying an aneurysm about the size of a hen's egg. It was apparently an aneurysm of a branch of the circle of Willis, probably the posterior cerebral artery. A part of its wall was calcified; there was a strong pulsation. The patient died two days after the craniotomy. Necropsy showed the venous side of the aneurysm to be formed by the great cerebral vein, while the arterial supply was the posterior cerebral and choroidal arteries. As in previously reported cases, internal hydrocephalus was the only significant clinical feature.

Gastroenterology, Baltimore

5:1-84 (July) 1945

Search for Symptomless Gastric Cancer in 500 Apparently Healthy Men of 45 and Over. M. E. Dailey and E. R. Miller.—p. 1.
Hyperalimentation Treatment of Peptic Ulcer with Amino Acids (Protein Hydrolysate) and Dextri-Maltose. Co Tui, A. M. Wright, J. H. Mulholland, T. Galvin, I. Barcham and G. R. Gerst, with technical assistance of Lilly Schmidt, L. Sutherland and Frieda Wolf.—p. 5.
Esophagus: Review of Literature for 1944. E. B. Benedict.—p. 18.
Do Aloes and Podophyllum (Carter's Little Liver Pills) Increase Flow of Bile into Duodenum? A. C. Ivy, J. A. Roth and M. Gutmann.—p. 27.
Passage of Air Through Gastric Wall During Gastroscopy, with No Wound Demonstrable Three Hours Later. R. Schindler.—p. 34.
Rate of Progress of Inert Material Through Small Intestine. E. J. Van Liere, J. C. Stickney and D. W. Northup.—p. 37.
Simple Method for Uniform Production of Gastric Ulceration in Rat. H. Shay, S. A. Komarov, S. S. Fels, D. Meranze, Margot Gruenstein and H. Siplet.—p. 43.

Illinois Medical Journal, Chicago

88:173-220 (Oct.) 1945

Global Disease. D. J. Davis.—p. 186.
Alcoholism, a Medical Problem. R. S. Sabine.—p. 194.
Public Assistance for the Blind in Illinois. R. H. Hilliard.—p. 199.
Spirochetes in Feces. G. H. Gowen.—p. 202.
Examination of Strabismus Patients, with Indications for Treatment. G. Guiber.—p. 203.

Journal of Clinical Investigation, Boston

24:611-774 (Sept.) 1945. **Partial Index**

Effect of Continuous Intravenous Administration of Histamine on Basal Metabolism in Human Beings. G. A. Peters, B. T. Horton and W. M. Boothby.—p. 611.
Liver Function Tests in Chronic Relapsing Vivax Malaria. S. W. Lippincott, L. D. Ellerbrook, W. B. Hesselbrock, H. H. Gordon, L. Gottlieb and A. Marble.—p. 616.
Lipids of Serum and Liver in Patients with Hepatic Diseases. Evelyn B. Man, B. L. Kartin, S. H. Durlacher and J. P. Peters.—p. 623.
Electrophoretic Changes in Serum Protein Patterns of Patients with Scarlet Fever and Rheumatic Fever. V. P. Dole, R. F. Watson and S. Rothbard, with technical assistance of Esther Braun and K. Winfield.—p. 648.
Chemical, Clinical and Immunologic Studies on Products of Human Plasma Fractionation: XXIV. Studies on Nutritive Value of Human Plasma Fractions. D. M. Hegsted, Alice L. Hay and F. J. Stare.—p. 657.
Id.: XXV. Preparation of Anti-A Isoagglutinin Reagents from Mixed Blood of Groups O and B. M. Melin.—p. 662.
Treatment of Experimental Hypoparathyroidism in Dogs. E. W. McChesney and N. J. Giacomino.—p. 680.
Electrocardiograms in Traumatic Shock in Man. C. H. Burnett, E. F. Bland and H. K. Beecher.—p. 687.
Quantitative Electroencephalographic Studies of Anoxia in Humans: Comparison with Acute Alcoholic Intoxication and Hypoglycemia. G. L. Engel, J. P. Webb and E. B. Ferris.—p. 691.
Studies in Blood Coagulation: Coagulation Properties of Certain Globulin Fractions of Normal Human Plasma in Vitro. F. H. L. Taylor, C. S. Davidson, H. J. Tagnon, M. A. Adams, A. H. MacDonald and G. R. Minot.—p. 698.
*Coagulation Defect in Hemophilia: Effect in Hemophilia of Parenteral Administration of Fraction of Plasma Globulins Rich in Fibrinogen. G. R. Minot, C. S. Davidson, J. H. Lewis, H. J. Tagnon and F. H. L. Taylor.—p. 704.
Increased Plasma Volume in Cardiac Insufficiency: Its Correlation with Rightsided Failure. G. A. Perera.—p. 708.
Solar Heat Load: Its Relationship to Total Heat Load and Its Relative Importance in Design of Clothing. H. F. Blum.—p. 712.
Serum Iodine of Euthyroid Subjects Treated with Desiccated Thyroid. D. S. Riggs, Evelyn B. Man and A. W. Winkler.—p. 722.
Serum Iodine in Hypothyroidism Before and During Thyroid Therapy. A. W. Winkler, D. S. Riggs and Evelyn B. Man.—p. 732.
Type Specific Meningococcic Agglutinins: II. Relationship of Titers to Course of Disease. Carolyn R. Falk and E. Appelbaum.—p. 742.
Effect of Salicylates on Electrolyte Structure of Blood Plasma: II. Action of Therapeutic Doses of Sodium Salicylate and of Acetylsalicylic Acid in Man. G. M. Guest, S. Rapoport and C. Roscoe.—p. 770.

Effect in Hemophilia of Globulins Rich in Fibrinogen.—Minot and his associates demonstrated that normal human plasma essentially free from formed elements, fibrinogen and prothrombin can cause a great reduction in the coagulation time of the blood in hemophilia when administered intravenously or intramuscularly. Such activity was associated with the plasma

euglobulin of normal plasma and was deficient in hemophilic blood. Administration, intravenously or intramuscularly, of small amounts of the globulin fraction (fraction I) of pooled normal human plasma reduced the blood coagulation time of hemophilic blood toward or to normal values in 15 out of 16 instances in which it was employed. One of these patients responded to as little as 11.5 mg. of the globulin. In 1 patient the effect of the intramuscular administration of 125 mg. of the protein was minimal. The dosage for therapeutic use has not been established, but 200 to 600 mg. of the globulin has an effect equal to that obtained by 80 cc. of fresh plasma or 100 cc. of whole blood.

Journal of Urology, Baltimore

54:221-355 (Sept.) 1945. **Partial Index**

Renal Adenoma: Case Report. A. Strauss.—p. 221.
*Prognosis of Renal Tuberculosis, Treated by Nephrectomy, and Outlook of Patient Who Is Considered Unsuitable for Operative Treatment. R. M. Nesbit, W. A. Keitzer and J. M. Lynn.—p. 227.
Effect of Renal Pelvic Lavage with Cetylpyridinium Chloride on Urinary Tract Infection and Urolithiasis. W. J. Erickson.—p. 235.
Secondary Ureterosigmoidostomy. S. F. Wilhelm and S. Freed.—p. 241.
*Cystoscopic Treatment of Stones in Ureter, with Special Reference to Large Calculi, Based on Study of 1,550 Cases. R. L. Dourmashkin. —p. 245.
Treatment of Bladder Dysfunction After Neurologic Trauma. L. G. Lewis.—p. 284.
Actinomycosis of Testicle: Case Report. D. H. Schneider.—p. 296.
Urinary Schistosomiasis: Report of 2 Cases in Maine. C. N. Peters, R. L. Huntress and J. E. Porter.—p. 301.
Multiple Primary Tumors. W. G. Hayward.—p. 307.
Plan for Management of Anuria. J. K. Lattimer.—p. 312.
*Chyluria: Clinical, Laboratory and Statistical Study of 45 Personal Cases Observed in Hawaii. S. Yamauchi.—p. 318.
Clinical Observations on Gonorrhea in Male in Sicily: Report of 137 Consecutive Cases Treated with Penicillin. R. C. Crowell, S. Propp and B. F. Hoopes.—p. 348.

Prognosis of Renal Tuberculosis.—Nesbit and his associates present data on 260 cases of genitourinary tuberculosis observed for five years or longer. Males predominated over females in a ratio of 2:1. The urine in about one third of the patients was secondarily infected by organisms other than the tubercle bacillus. About half of the nephrectomized patients are living (an average of eleven years after operation) while 81.3 per cent of patients not operated on died (in an average of three years). They were unable to demonstrate that genital complications in the male increased the mortality of renal tuberculosis. The higher death rate among males is probably due to the higher mortality of tuberculosis generally in this group. The following three facts were found to be statistically significant: 1. In nephrectomized patients a lower rate of survival will be present in the group having acid fast bacilli demonstrated by guinea pig inoculation in the urine from the unoperated kidney than in those with normal urine on the unoperated side. 2. The survival of women is greater than that of men in urinary tuberculosis. 3. The mortality rate of genitourinary tuberculosis is adversely influenced by the presence of bone and joint or pulmonary lesions.

Cystoscopic Treatment of Stones in Ureter.—Dourmashkin has employed metallic dilators (tunneled bougies) for treatment of stones in the lower end of the ureter, and rubber bag dilators for calculi in the upper two thirds of the ureter. In a series of 1,550 cases of stones situated at all levels of the ureter and renal pelvis, cystoscopic manipulation of 1,253 resulted in 1,171 cases (93.5 per cent) in the expulsion of the stone without an instance of ruptured ureter or mortality resulting from instrumentation. The cases were divided into two groups: 689 with small stones less than 5 mm. in width and 564 with large stones, 5 mm. and more in width. In the small stone group the stones were passed in 99.7 per cent of the cases and in the large stone group in 85.9 per cent. Ample room for the downward passage of the stone was achieved by dilating the lower end of the ureter with metallic bougies and by using rubber bags at the higher levels. Passage of an ordinary catheter was sufficient to induce the expulsion of a small stone in the majority of cases. There are a number of mechanical factors which maintain renal drainage in ureteral stone cases. For this reason renal stones can be present for considerable lengths of time without appreciable renal injury. The majority of patients were treated in ambulatory fashion. Indwelling multiple catheters do not provide adequate dilatation in large stone cases and are apt to produce renal infection. In Dourmashkin's opinion forcible extraction of stones is contraindicated, as the same results may be obtained by more conservative methods without the danger of injury to the ureter.

Chyluria.—Yamauchi believes that physicians in the United States will encounter cases of chyluria among men and women returning from Filaria infested regions. The 45 patients presented by the author were all residents of Hawaii (where filariasis is not endemic) who had been exposed previously to filariasis. Clinical, laboratory and pyelographic studies based on the analysis of the records of these 45 cases of chyluria are compared and correlated with those recorded in the literature. The long period elapsing between exposure to Filaria and the onset of chyluria, the absence of eosinophilia and several other factors indicate that filariasis probably predisposes to this condition but does not actually initiate it. Urinary stasis has been considered to be the exciting cause of chyluria. Fornix rupture caused by urinary stasis results in a lymphaticourinary communication, and chyle appears in the voided urine. Minimal pathologic changes sufficient to form varices are probably present in the lymphatics without definite obstruction to the large retroperitoneal lymphatic vessels and thoracic duct. The presence of fat granules in a colloidal state, the presence of albumin, erythrocytes and lymphocytes, the pyelographic injection of the renal and perirenal lymphatics frequently associated with fornix rupture and pyelovenous reflux and the control of the condition by repeated intrapelvic lavages with sclerosing solutions indicate a lymphaticourinary fistula at the fornix of the calices. The control of chyluria can be accomplished by repeated intrapelvic lavages of silver nitrate solutions through inlying catheters. Urinary stasis must be removed. Fat must be restricted in the diet after such lavages.

Kansas Medical Society Journal, Topeka

46:325-360 (Oct.) 1945

Management of Emboli and Thrombophlebitis. L. S. Nelson.—p. 326.
Intestinal Obstruction in the Newly Born Due to Error in Rotation of Midgut Loop During Fetal Development: Presentation of 2 Cases. D. N. Medearis.—p. 328.

46:361-396 (Nov.) 1945

Traumatic Chylothorax. H. J. Davis.—p. 361.

Medical Annals of District of Columbia, Washington

14:443-482 (Oct.) 1945

Host Variation in Manifestation of Disease, with Particular Reference to Homologous Serum Jaundice in the Army of the United States. L. W. Parr.—p. 443.
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14:483-530 (Nov.) 1945

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Acute Anterior Poliomyelitis: Diagnosis, Differential Diagnosis and Treatment of Bulbar Paralysis and Respiratory Failure. L. K. Sweet. —p. 501.

Medicine, Baltimore

24:219-338 (Sept.) 1945

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Cutaneous Arterial Spider: Survey. W. B. Bean.—p. 243.
Chemical Separation and Clinical Appraisal of Components of Blood. E. J. Cohn.—p. 333.

Missouri State Medical Assn. Journal, St. Louis

42:621-676 (Oct.) 1945

Thiouracil: Its Use in Hyperthyroidism. D. L. Sexton and M. Levy. —p. 621.
The Patient Diagnoses the Doctor. J. R. Van Pelt.—p. 639.

42:677-748 (Nov.) 1945

Intestinal Obstruction: Two Cases of Unusual Etiology. V. T. Williams and H. B. Walker.—p. 693.
Continuous Drip Pentothal Sodium with Supplementary Anesthesia. Sister M. Cyrilla, O.S.B.—p. 694.

Physiological Reviews, Baltimore

25:573-716 (Oct.) 1945

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Present Views on Mode of Action of Acetylcholine in Central Nervous System. W. Feldberg.—p. 596.
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81:465-592 (Nov.) 1945

*Osteoid Osteoma, with Case Reports. J. F. Hamilton.—p. 465.
Bacteriologic Studies of Clostridium Welchi Infections in Man, with Special Reference to Use of Direct Smears for Rapid Diagnosis. H. M. Butler.—p. 475.
*Experimental Evaluation of American Commercial Bivalent and Pentavalent Gas Gangrene Antitoxins. I. C. Hall.—p. 487.
*Study of Late Symptoms of Cases of Immersion Foot. E. G. Fausel and J. A. Hemphill.—p. 500.
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Struma Lymphomatosa, Struma Fibrosa and Thyroiditis. J. A. Schilling.—p. 533.
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Evaluation of Coffey I Method for Ureterointestinal Anastomosis. V. F. Marshall and J. S. Gardner.—p. 559.
Surgery of Mandible: the Ameloblastoma. L. T. Byars and B. G. Sarnat.—p. 575.
Biologic Investigations of New Absorbable Sponge. J. T. Correll, Hazel R. Prentice and E. C. Wise.—p. 585.

Osteoid Osteoma.—Hamilton presents 5 cases of osteoid osteoma which demonstrate that the disease may be readily and correctly diagnosed. It is frequently confused with sclerosing nonsuppurative osteomyelitis of Garré, Brodie's bone abscess and osteogenic sarcoma. The diagnosis can be made, provided the pathologic process has developed to the point where there is roentgenographic evidence to support the clinical findings and the physician is aware of the possibility of an osteoid osteoma and knows the symptomatology, physical findings and x-ray evidence produced by the pathologic process. Localized pain of a dull, aching character, most annoying at night, with tenderness over the site of the lesion usually confined to an area from 1 to 2 cm. in diameter, is most characteristic. The majority of the patients are in the second or third decade of life. A typical roentgenogram of an osteoid osteoma reveals an oval to round area from a few millimeters to 1 or 2 centimeters in diameter, the center of which presents small areas of rarefaction and condensation. Surrounding this is a narrow zone of condensation, and just outside of this is a zone of rarefaction. The surrounding parent bone is, as a rule, sclerosed for a variable depth. Occasionally the first picture may be negative. This type of case should be restudied by x-rays at a later date, thus giving time for the lesion to develop. The prognosis is uniformly good provided all of the lesion is excised. On the contrary, if it is not removed completely, pain will continue or recur.

Bivalent and Pentavalent Gas Gangrene Antitoxins.—Hall believes that gas gangrene serum is not needed for wounds which receive prompt adequate surgery. The principal value of gas gangrene serum is prophylactic to prevent or delay anaerobic infection until adequate surgery can be secured, but it cannot take the place of adequate surgery. It has therapeutic value when used in adequate dosage as an adjunct to surgery in the treatment of malignant edema and gaseous gangrene due to anaerobic bacilli. Hall studied seven brands of gas gangrene antitoxin. Six of these were bivalent and were labeled to contain 10,000 units each of Bacillus perfringens and Bacillus sordellii antitoxins. One was pentavalent and labeled to contain in addition 3,000 units of Bacillus histolyticus antitoxin and 1,500 units each of Bacillus novyi and Bacillus sordelli antitoxins. All of these antitoxins were first tested against a weak toxin of B. perfringens, which generally killed guinea pigs in a dose of 1 cc. but still produced lesions in a dose of 0.05 cc. Five of the seven brands of serum gave complete prophylactic protection against 1 cc. of this toxin in doses of 0.01 cc. or larger; all 5 failed in a dose of 0.001 cc. One gave complete protection in a dose of 0.1 cc. but failed at 0.01 cc., while another gave complete protection at 0.1 cc. and failed irregularly at 0.01 cc. The pentavalent serum was shown to have not only prophylactic but therapeutic action against infections in guinea pigs with a virulent culture of B. perfringens. The immunity conferred by 1 cc. of five antitoxins injected along with 1 cc. of B. perfringens was shown to persist for at least a week when challenged with at least 10 lethal doses of B. septicus culture. The pentavalent serum was shown to have prophylactic values in a dose of 0.1 cc. and therapeutic values in a dose of 1 cc. at twenty-seven hours against at least 100 lethal doses of B. novyi. It had prophylactic values in a dose of 0.1 cc. against at least 10 lethal doses of Bacillus histolyticus. The author concludes that there is no reason to doubt the prophylactic value of seven American gas gangrene antitoxins against the anaerobic infections for which they were intended. One of these serums has been shown to have good therapeutic values against B. perfringens and B. novyi but only slight therapeutic value against B. septicus under the conditions of a possibly too severe test.

Late Symptoms of Immersion Foot.—A group of 65 patients were studied by Fausel and Hemphill fourteen months after the occurrence of immersion foot. Of these, 49 had complaints and 42 had abnormal physical findings associated with chronic peripheral vascular disease secondary to immersion foot. Secondary symptoms following immersion foot are common and more persistent than usually thought. The main complaints are rest pain, numbness of the legs or feet, subjective coldness of the legs or feet and increased perspiration of the extremities. Abnormal physical aspects, particularly plantar ischemia, development of superficial varicosities and decreased peripheral arterial pulsation of the dorsalis pedis artery, usually unilateral and corresponding to the primarily affected extremity, exist in a surprisingly high proportion of patients who have complaints. The authors think that these complaints are on the basis of fibrosis of the extremity secondary to the initial inflammatory reaction after immersion rather than to secondary angiospasm. The persistence of peripheral vascular disease secondary to immersion foot should be brought to the attention of surgeons dealing with immersion foot in view of the fact that these cases may be a source of future persistent disability.

United States Naval Med. Bulletin, Washington, D. C.

45:819-1028 (Nov.) 1945

War Wounds of Lips and Cheeks. G. V. Webster.—p. 819.
Plastic Repair of Radiation Ulcers of Sole. P. W. Greeley.—p. 827.
Organization of Medical Service in the U. S. S. R. Navy. F. Andreyev.—p. 831.
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Posttraumatic Urinary Suppression—Shock as Causative Entity, with Review of Rh Factor and Report of Cases. H. L. Pugh.—p. 859.
Health of Liberated Naval Personnel: Report from Luzon. O. C. Hendrix, J. D. Houghton, H. O. Schneider and J. E. Edwards.—p. 874.
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Rapid Method for Primary Isolation and Identification of Neisseria. A. M. Weckstein.—p. 889.
Neuropsychiatric Questionnaire for Group Examining. H. M. Hildreth and J. M. Hill.—p. 895.
Nutritive Value of Naval Food. C. M. McCay, F. H. Davis, R. A. Gortner Jr., Gladys E. Haugen and June H. Sullivan.—p. 903.
Reduction of Complete Transverse Fracture of Edentulous Maxilla. H. N. Stevenson and F. A. Tuoti.—p. 910.
Treatment of Bacillary Dysentery Carriers with Sulfonamides. R. W. Getty and others.—p. 914.
Penicillin in Otitis Media: Treatment of Disease and Its Complications. S. von Christierson.—p. 919.
Penicillin in Treatment of Streptococcal Empyema. C. J. Metcalf.—p. 926.
Penicillin in Primary Atypical Pneumonia: Report of 28 Cases. S. T. Allison.—p. 930.
Sudden Decrease in Central Vision: Its Emergency Nature and Treatment. R. W. ter Kuile.—p. 933.
Emergency Blood Transfusions on Hospital Ships in War Zones. J. C. Norris.—p. 938.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Brain, London

68:1-78 (Nov.) 1945

Changes in Nervous System in Acute Porphyria. D. Denny-Brown and D. Sciarra.—p. 1.
Electroencephalography in Prognosis of War Neurosis. Mollie E. Heppenstall, D. Hill and E. Slater.—p. 17.
Arterial Relations of Internal Auditory Meatus. S. Sunderland.—p. 23.
Vascular Diseases of Nervous System. C. D. Aring.—p. 28.
Traumatic Injuries of Peripheral Nerves: I. Simple Compression Injuries of Radial Nerve. S. Sunderland.—p. 56.

Journal of Pathology and Bacteriology, Edinburgh

57:285-396 (July) 1945

Influence of Substrate on Variation of Brucella Bronchiseptica. L. Dickinson.—p. 285.
Study of Protective Factors in Heterospecific Blood Group Pregnancy and Their Role in Prevention of Hemolytic Disease of the Newborn. G. H. Tovey.—p. 295.
Non-Mannitol Fermenting Dysentery Bacilli. J. D. MacLennan.—p. 307.
Histologic Study of Lungs of Mice Infected with Typhus Rickettsiae. W. Nyka.—p. 317.
Factors Influencing Preservation of Stored Red Cells. J. F. Loutit.—p. 325.
Further Observations on Adenosine Equivalent of Blood of Rabbits Following Lethal Forms of Tissue Injury. H. B. Stoner and H. N. Green.—p. 337.
Gross Defects in Muscular and Elastic Coats of Larger Cerebral Arteries. R. Carmichael.—p. 345.
Relative Effects of Dietary Constituents and Other Factors on Calculus Formation and Gingival Disease in the Ferret. J. D. King and R. E. Glover.—p. 353.
Congenital Malformations of Esophagus. Katherine J. Guthrie.—p. 363.
Formation of Nucleus of Stone in the Urinary Passages. Greta Hammarsten.—p. 375.
*Simple Method of Testing Sensitivity of Wound Bacteria to Penicillin and Sulfathiazole by Use of Impregnated Blotting Paper Disks. D. C. Morley.—p. 379.

Simple Test for Sensitivity of Wound Bacteria.—Blotting paper disks impregnated with penicillin solutions have been used by various workers to detect bacterial sensitivity to penicillin. Usually the disks are laid wet on the surface of an inoculated agar plate or are impregnated while lying on the agar by dropping penicillin solution on them. Blotting paper disks impregnated with penicillin before drying appeal to Morley as more convenient to use because they dispense with the need of maintaining suitable dilutions of penicillin, which must be frequently renewed because of their instability. As the dried disks can be stored over a long period and are always ready for use, they are likely to be most valuable in small laboratories in which a test of sensitivity to penicillin is a comparatively rare event. A similar method has been tried to detect sensitivity to sulfonamides. Although the implications of a negative result have not been determined, this method reveals a certain number of strains which are sensitive to sulfathiazole. It is quick and convenient.

Lancet, London

2:453-484 (Oct. 13) 1945

On Nothing in Particular: Extracts from Inaugural Address to Students of London School of Medicine for Women. L. Moran.—p. 453.
Military Psychiatric Casualties: Experience with 12,000 Cases. H. Palmer.—p. 454.
*Hepatorenal Syndrome Treated with Choline Chloride. J. A. Barclay and W. T. Cooke.—p. 458.
Sigmoidoscopy in Amebic Dysentery. C. F. J. Cropper.—p. 460.
*Penicillin in Skin Conditions in the Army. F. F. Hellier and G. A. Hodgson.—p. 462.
Through and Through Bullet Wounds of Mediastinum, with Recovery. T. St.M. Norris.—p. 464.

Hepatorenal Syndrome Treated with Choline Chloride.—A man aged 27, who in childhood had had a mild jaundice, was admitted to a field dressing station in a state of severe anxiety and exhaustion. He was given barbital for five days but was still depressed. During the next three days he was given phenobarbital and in the next two days more barbital and sodium amytal. He became unconscious and anuric. After four doses of picrotoxin at two hour intervals he returned to consciousness. He passed three stools which contained blood and mucus and vomited six times but passed no urine. Dysentery was considered possible because of severe abdominal pain. He was given sulfaguanidine by mouth and dextrose in isotonic solution of sodium chloride intravenously. No urine was passed, vomiting continued and the abdomen became jaundiced. There was continued hiccup and vomiting, and jaundice became deeper. Choline was given and later methionine and choline, which resulted in gradual improvement and recovery. Barclay and Cooke state that the cause of failure of the liver and kidney function of this patient is obscure. The previous attack of jaundice probably rendered him more susceptible to hepatitis. Jaundice and hepatic degeneration have been described in barbiturate poisoning and some of these patients have had renal damage. Although liver damage of the degree seen in this patient is rare in barbiturate poisoning, this seems to be the most likely explanation.

Penicillin in Skin Conditions.—In the early days of penicillin treatment the drug was restricted to infectious conditions of the skin such as impetigo, ecthyma, folliculitis and sycosis. Later, when more penicillin was available, it was used to treat the infective element in septic eczema, seborrheic dermatitis and sulfonamide dermatitis and was used parenterally for boils and carbuncles. Penicillin spray has been used mostly. The patients were usually sprayed three times a day with ordinary throat spray. A solution of 200 to 500 units per cubic centimeter was used. With a strength of less than 200 units per cubic centimeter the failure rate increased, but no advantage seemed to be gained by increasing the strength above 500 units per cubic centimeter. The use of too strong a solution may even lead to sensitization or at least irritation. Penicillin emulsion made up with 30 per cent Lanette wax in water and containing 200 to 500 units per gram was effective in the same types of conditions as the spray but was particularly useful in infected weeping areas which need a dressing. Hellier and Hodgson have used penicillin emulsion successfully in outpatient clinics, and it will probably be the method of choice in civil practice. Parenteral administration of penicillin has been used in the treatment of carbuncles, severe or recurrent boils and streptococcic infections around the ear.

Khirurgiya, Moscow

2:1-96, 1945. **Partial Index**

*Anaphylactic Shock in Intravenous Infusions of Antigangrenous Serum. Borisenko-Mitlash and V. I. Popov.—p. 7.
Treatment of Wounds with Chloracid. N. V. Antelava.—p. 16.
Chlorethylideno Methylen Narcosis. D. M. Rossiisky.—p. 19.
Secondary Sutures and Epidermal Plastics in Units of Front Region. M. G. Taborissky.—p. 23.

Anaphylactic Shock Following Intravenous Antigangrene Serum.—Borisenko-Mitlash and Popov state that infusions of large amounts of antigangrene serum are not infrequently complicated by anaphylactic reactions despite all precautionary measures. They have observed in a number of cases typical anaphylactic shock terminating in death. They have seen instances of early shock following the introduction of the first few drops of the serum, as well as instances in which shock occurred one to four hours after the infusion. These late fatalities due to anaphylactic shock were erroneously considered by many as deaths due to toxemia of gas gangrene. Besredka's law is not infallible as far as prophylaxis of serum infusion is concerned. His method of desensitization, which consists in injection of a small amount of serum intramuscularly one and one-half to two hours previous to the infusion, is quite reliable in intramuscular, intraperitoneal and subdural injections of serum. It is less reliable in intravenous infusion of large doses of heterogenous serum. Substitution of the intramuscular method of administration of serum for the intravenous lowered the mortality by from 7 to 10 per cent. Prophylaxis of anaphylactic shock in intravenous infusions of large doses of antigangrene serum can be more successfully accomplished by the simultaneous employment of two methods, the desensitization according to Besredka and narcosis with 0.25 per cent solution of evipal in 400 cc. of isotonic solution of sodium chloride with 1 cc. of ephedrine. The infusion must be performed slowly. The nature of the reactions following intravenous infusions of antigangrene serum requires further elucidation.

Book Notices

What People Are: A Study of Normal Young Men. By Clark W. Heath, in collaboration with Lucien Brouha, Lewise W. Gregory, Carl C. Seltzer, Frederic L. Wells and William L. Woods. The Grant Study, Department of Hygiene, Harvard University. Cloth. Price, $2. Pp. 141, with 8 illustrations. Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1945.

This book is to be regarded as a brief introduction to the point of view of the Harvard Grant Study and the methods used to study superior normal young men from 17 to 24 years of age at Harvard University in order to discover the physical, mental and social traits and characteristics related to relative success or failure some fifteen to twenty years hence. It is a study of normal behavior rather than of disease or abnormality.

The principle on which the study was founded is that the segment of the population which was successfully carrying on the work of the world had lacked the attention it merited by investigative technic even now available. It points out that the concept of "normal" is too often the idea of absence of abnormality.

The study is distinguished by the scope of the appraisal methods in which experts from various fields have appraised their normal personality traits, adjustment to environment, socioeconomic status, mental ability, morphology, physiology and pathology. A large number of measurements or ratings were made under each of these leads. The data cover 238 carefully selected cases appraised during the first four years of study, 1938 to 1941 inclusive. The appendixes give the range, mean and standard deviation of these measurements; also the frequency and percentage for characteristics which were rated but not measured. No statistical results are included to show the quantitative relationships between the traits, abilities, characteristics and performances measured. The approach in the main has been clinical, with each specialist relatively free to appraise the subjects in the manner best suited for his own field.

The aim is to continue the study indefinitely as an institution rather than operate a project limited in time and scope. The intention is to continue the validation of various tests by long-time follow-up and to develop new procedures as they may be found necessary. The continued objective will be to discover the elements making for integration, drive and economic success in life and to verify the hypothesis that leaders of people usually rise from the energetic, well and fit types with higher quality for health than from the opposite. So far there are no conclusions along this line, and there cannot be until the careers of the men are followed.

The selection of subjects was limited to those men who were among the best conformers to social and scholastic disciplines as approved by the deans of their respective colleges. This limits the study tremendously, as there appears to be no control group of less able students. The preconception is that the leaders will arise from the sample selected. A fundamental limitation is that the basic measurements are almost devoid of measurements now made in physical education: motor skill, strength, posture, balance, flexibility, agility, power and some specific aspects of muscular and cardiovascular endurance which are better than the tests used. Analysis of weight by bone, muscle and fat quotas, using appropriate prediction equations for each, composite dynamometer strength per pound of weight, heartogram, electrocardiogram, vital capacity for surface area, expiratory force and breath holding after standardized exertion are other possible tests. The appraisal of the motor qualities seems inadequate to experts in physical education. If health is related to health habits, athletic participation, recreation and measurable aspects of fitness, there should be more careful appraisal of these traits and qualities because of the fundamental hypothesis set up to be verified or rejected. Amount and type of exercise and a complete athletic record seem important enough to record in some detail.

The investigation of mental characteristics impresses one as having been carried out with considerable regard for precision and reliability. In the field of abilities and achievements the research leaves little for criticism or suggestion except that, if special abilities are to be measured at all, the use of Thurstone's measure of primary mental abilities would have been more defensible than the *ad hoc* special ability measures employed.

In the field of personality description, however, it is unfortunate that no attempt has been made to measure with respect to the half dozen or more clearly defined personality factors revealed as basic for the factor analytic research of the past fifteen years. Even if these assessments had to be made by behavior ratings, by questionnaires or by dynamic projection tests of the thematic apperception type it would have been better —for any attempt at future alinement of findings with general psychologic knowledge—than to depend on a rather ill assorted set of trait ratings or the broken reed of the Rorschach test.

Diagnostic Procedures and Reagents: Technics for the Laboratory Diagnosis and Control of the Communicable Diseases. Second edition. Fabrikoid. Price, $4. Pp. 549, with illustrations. New York: American Public Health Association, 1945.

This is a complete revision of the first edition with the addition of nine new chapters. There are no numbers given to the chapters, but twenty-eight subjects are discussed by nearly that number of different authors, although some authors have been responsible for more than one chapter. The chairman of the Standard Methods Committee, William D. Stovall, had the task of collecting the manuscripts. He, with Lois Almon, also prepared the chapter on pathogenic fungi. As is to be expected, there is no uniformity in the style of writing or in the arrangement of the subject matter. However, each author has conscientiously reviewed the literature, and the long lists of references are valuable guides to further study of any of the technical procedures briefly described. While the title page indicates that the technics for the laboratory diagnosis and control of communicable diseases make up the subject matter, the different authors, depending on their experience, consider the topics differently. One author may stress technic for the identification of organisms, formulas and new methods as well as old, while another considers interpretation of laboratory findings as applied to clinical diagnosis. Control measures, such as quarantine regulations in diphtheria, meningococcic infections, pertussis and streptococcic infections, are discussed. Procedures for prophylaxis and immunization are not given, probably because they are not of diagnostic significance. However, the inclusion of such information would have been helpful to health officers, clinical pathologists and other physicians who are called on to keep the medical profession and the public informed on timely methods of preventive medicine. While this book can in no sense be considered a textbook of laboratory methods, it is a useful guide to the literature on the laboratory diagnosis of communicable diseases.

Dental Chronology: A Record of the More Important Historic Events in the Evolution of Dentistry. By Hermann Prinz, A.M., D.D.S., M.D. Cloth. Price, $8. Pp. 189, with 97 illustrations. Philadelphia: Lea & Febiger, 1946.

This is a small book containing the dates of what the author regards as important events in the evolution of dentistry. It also lists the names of persons who are thought to have made notable contributions to its development. The contents are divided into three periods: (1) antiquity, to the year 1000, the middle ages, from 1000 to 1728, and modern times, since 1728. For the most part the events selected are listed by dates with little or no comment as to their significance. One is led to wonder why certain events and certain persons are listed and why others are omitted, for there seems to be some glaring omissions even allowing for the fact that in any compilation such as this there could always be differences of opinion as to what should or should not be included. For example, no mention whatever is made of men or events connected with either the first or the second world war, which is astonishing, for in both wars remarkable advances were made which profoundly influenced the evolution of dental practice and dental teaching. The contributions of certain dentists in both wars were of such distinction as to deserve a place in any dental chronology. The author does state that "the book does not make a pretense of serving as a substitute for a competent history." For those interested in the date of occurrence of particular events in dental history this book might prove to be useful for reference.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VIRAL INFLUENZA

To the Editor:—**For several months I have been seeing an upper respiratory infection which is different from any previously seen. It vaguely resembles atypical virus pneumonia but simply does not progress into the lungs. It differs from an ordinary common cold in a number of respects, although it is quite similar. A few observations of characteristics which distinguish this ailment are its great contagiousness, the apparent susceptibility of all small children, the mildness in infancy and greater severity in later childhood, the extreme nervous irritability which attends it, the absence of coryza at first followed by an irritating mucoid nasal discharge later, a tendency to epistaxis, the almost universal hemorrhagic appearance of the tympanic membrane and the frequent bleb formation on the drum with severe pain, the comparatively mild pharyngitis, the intractable late cough, the recurrence or perhaps reinfection due to immunity of short duration, secondary anemia out of proportion to the expected effect of the illness, susceptibility of the air passages to changes of temperature for long periods and, last, the few serious complications and sequelae and the low mortality up to this point. The disease is increasing in severity rapidly. I have observed an increase in the number of cases in which abdominal pain, vomiting and diarrhea occur about the fourth or fifth day after onset. My facilities for bacteriology are limited to the identification of what might be termed the "major organisms." Throat and nose cultures show only a gram-positive diplococcus either in pure culture or with short chain streptococci. I am sure that this is not due to either of these organisms. The gram-negative bacillus associated with influenza has been lacking. I did not see the influenza epidemic of 1917 and 1918, but from the descriptions heard and read I should say that the infection described more closely resembles it than does the infection of the upper respiratory tract which has been loosely called "flu" during my medical life. Somewhere adequate bacteriologic studies have undoubtedly been done. Will you give me an opinion and the probable diagnosis? In favor of the diagnosis of influenza is the fact that 2 patients who followed a fairly typical course developed unquestioned influenzal meningitis, 1 now in the process of recovery with anti-hemophilus type B serum therapy. I am entirely convinced that good results are not forthcoming from sulfonamides or penicillin.**

J. M. Albergotti Jr., M.D., Orangeburg, S. C.

ANSWER.—The first statement in the query has a familiar ring in the ears of an epidemiologist. When periodic epidemic waves of a contagious disease appear after long intervals, the disease is apt to be regarded as a new one and "different from any previously seen." The experience described in the query was the same in Philadelphia and elsewhere in December and January. Evidence of infection with the B virus of influenza was discovered in many patients locally and elsewhere in the country. Influenza B virus was probably the cause of the epidemic, as the inquirer suspects, because of its contagiousness, prevalence in childhood, mild pharyngitis, irritability, myringitis, cough, few complications and the recurrences as described. Among adults the symptoms were similar. In adults the pharynx was often intensely red and edematous but gave little discomfort; headache, general aching, sweating, paroxysmal coughing and irritability or depression were prominent, as were recurrences after several days or even two weeks.

In addition to the clinical picture described, there were numerous cases of viroid or of viral pneumonia (typical atypical [sic] pneumonia). But whether these were caused by the B virus of influenza or other ones was not determined. As noted in the query, there were also instances of viral dysentery, commonly called nausea, vomiting and diarrhea both with and without evidence of involvement of the upper respiratory tract, like those which occurred in epidemic form in Philadelphia in 1943 and 1944 (Reimann, H. A.; Hodges, J. H., and Price, Alison H.: Epidemic Diarrhea, Nausea and Vomiting of Unknown Cause, THE JOURNAL, Jan. 6, 1945, p. 1).

The discussion illustrates the present confusion in diagnosing different but similar clinical entities which cannot be further clarified until methods for the demonstration of the respective etiologic agents are available. Epidemics of influenza with or without pneumonia, of viroid with or without pneumonia, of viral dysentery and of the ill defined group of the common colds are seasonal and may overlap. At present some of them can be diagnosed tentatively only by the predominance of characteristic symptoms, signs and laboratory evidence of the respective diseases. For influenza the Hirst red cell agglutination test, the complement fixation test and the isolation of the virus establishes diagnosis. For viroid the cold agglutination test is of value after the disease is over and perhaps the newly discovered virus of Eaton may eventually be isolated. For common colds and for viral dysentery the diagnosis depends on clinical and epidemiologic evidence alone, as described in the paper referred to. Ordinary bacteriologic cultures of the nose and throat are of no value in diagnosis.

The inquirer is in error when he states that the recognition of meningitis caused by Hemophilus influenzae (Pfeiffer's bacillus) supports a diagnosis of influenza. Pfeiffer's bacillus, the so-called influenza bacillus, has nothing to do with influenza as we now understand it to be caused by influenza viruses A and B and probably X or Y. The habit of loosely calling all minor febrile diseases "flu" should be stopped. Influenza is now an established etiologic entity and must be regarded as such for the sake of accuracy and in view of current use of specific prophylactic vaccine.

It is true that neither the sulfonamide compounds nor penicillin have any specific influence in viral infections of the kind in question.

It may be pointed out incidentally that streptomycin seems to be of value for meningitis caused by H. influenzae.

THE GAY TREATMENT FOR ASTHMA

To the Editor:—**I have heard recently of some special treatment for asthma that is given by Dr. Fred S. Gay of Biloxi, Miss. Can you tell me the nature of this treatment?**

M.D., Wisconsin.

ANSWER.—According to Dr. Gay, he accepts patients only by appointment and only a limited number at any time. He requests his patients to stay under his immediate observation for a week, after which they go home and continue treatment as he directs them. Dr. Gay says also that he is always glad to furnish the patients' family doctor with copies of the prescriptions he gives the patients. Dr. Gay states that he "never did advertise in any way and that the only way any one ever heard of him was from some patient he had treated."

Reports indicate that his methods have developed a considerable amount of interest among the medical profession and that some physicians have been visiting him to secure the details of his technic, and for that reason this subject is published in Queries and Minor Notes in THE JOURNAL.

In response to an inquiry Dr. Gay has written that he does not use any specific new method of treatment of asthma. He endeavors to correct any abnormality that may exist, paying particular attention to the gallbladder and kidneys.

Patients are carefully examined and given the medication which according to Dr. Gay's judgment is indicated in each individual case. Most patients are given some form of calcium, such as calcium lactate or some form of liquid calcium, such as Calmulsion, in varying quantities and a prescription containing Fowler's solution and potassium iodide in varying quantities figured according to age, weight and general condition of patient. To this is added where and if indicated small quantities of tincture digitalis or phenobarbital put up in a vehicle of plain water, sometimes sweetened and sometimes colored red with an inert coloring substance of no medical value. In addition he oftentimes gives an oil solution of amphetamine solution, 2 drachms to 2 ounces of light petrolatum for nose drops and insists that the intestinal secretions be kept acting well at all times, for which he recommends a tablet containing pure bile salts and cascara, such as Colopo Tablets, made by the G. W. Carnrick Company, or bile salts with cascarin, made by Parke Davis and Company.

Dr. Gay supplies the medicine to his patients in most cases and requests that they report their general condition, weight and other details to him by mail at regular intervals and directs them as to procedure over a period of two years or more and claims that more than 90 per cent of his patients report improvement and in a large percentage complete relief from asthma within a two year period. He uses no ephedrine nor opiates but allows all patients to take any temporary relief medicines at any time if needed, including epinephrine, aminophylline and ephedrine.

SIX YEAR OLD BOY SHOULD SLEEP ALONE

To the Editor:—**Is it harmful from a physical or mental standpoint for a boy aged 6 years to sleep with his father?**

M.D., New York.

ANSWER.—In general it is more healthful for a child to sleep alone, certainly from the point of view of emotional health. Although serious harm would probably not result from a 6 year old son sleeping with his father, it is poor mental hygiene in that the child is being placed in a situation which may provoke anxiety. The quite normal feelings of love, envy, jealousy and fear that any son may have toward his father may all be aggravated by such an arrangement. It is better for a child to sleep alone if the physical condition of the home will permit.

HEAT CRAMPS OCCURRING ONLY AT NIGHT

To the Editor:—A man aged 27 has had eight seizures in six years, usually coming at night and awakening him with nausea. Vomiting nearly always follows and occasionally diarrhea. Then in about thirty minutes he notes a stiffening of his fingers and slowly they go into extensor tetany. The legs and feet next go into extensor spasm. Then the abdominal muscles tighten and finally the facial muscles draw stiffly. The thorax has never been involved. When the attack is allowed to progress to its fullest extent it is extremely painful. There are never any headache, clonic convulsions, incontinence, cry, loss of consciousness, numbness, paresthesias or resultant paralysis. The first attack was in 1938 during hot weather, and salt was given orally and seemed to control the seizure. Since then the patient has asked for salt and is given intravenous solution, since oral salt makes him ill, and always obtains relief. It is not quite clear whether or not all attacks have been preceded by perspiration. Attempts to relieve attacks by calcium were useless. There has not yet been an opportunity to observe an attack, but plans are being made to obtain samples of blood for testing of the potassium, sodium, calcium and carbon dioxide combining power. D. I. Thompson, Captain, M. C., A. U. S.

ANSWER.—The symptoms are consistent with a diagnosis of heat cramps, a malady associated with loss of salt in the sweat, painful cramps in the voluntary muscle of the extremities and relief following replacement of sodium chloride. The age, sex, periodicity and environment likewise conform. Nausea and vomiting are unusual precursors but, if they occur, tend to aggravate the pathologic processes due to increased loss of electrolytes from the body. The pain in the muscles is the incapacitating feature of heat cramps. One should inquire whether the patient had been engaged in strenuous activity on the day prior to the onset of symptoms. Under such circumstances loss of sodium chloride in the sweat may have depleted the body content to a critical level. The muscle spasms are not usually referred to as tetany, and the flexors are more often affected than the extensors. As noted in the query, it would be desirable to determine the concentration of serum electrolytes, particularly serum sodium, calcium and carbonate. Idiopathic nocturnal cramps cannot be excluded from the evidence presented. A review of the literature on heat cramps by J. H. Talbott appeared in *Medicine* (**14**:323 [Sept.] 1935).

INCOMPATIBILITY OF CODEINE AND AMMONIUM CHLORIDE

To the Editor:—This inquiry concerns the use of codeine in sedative cough mixtures. It is generally stated in the pharmacology of codeine that it is incompatible with ammonium chloride and alkalis (the Merck Index, ed. 5, Rahway, N. J., Merck & Co., Inc., 1940, p. 159). Yet in Beckman's book (Beckman, Harry: Treatment in General Practice, ed. 4, Philadelphia, W. B. Saunders Company, 1942, p. 21) codeine and ammonium chloride are combined in a cough mixture. Then too, Goodman and Gilman (Goodman, Louis, and Gilman, Alfred: The Pharmacological Basis of Therapeutics, New York, Macmillan Company, 1941, p. 220) suggest that codeine may be profitably combined with the sedative expectorants without excluding ammonium chloride or the citrates.

Israel Pine, M.D., Belle Harbor, L. I., N. Y.

ANSWER.—Although ammonium chloride is stated to be incompatible with codeine preparations because of the liberation of ammonia, which would precipitate the alkaloid as a base, such mixtures as that cited by Beckman may be prepared by mixing solutions of the drugs, rather than the dry forms, and then adding the solvent. The permanence of such preparations is usually adequate for clinical use.

SULFONAMIDES

To the Editor:—When were the sulfonamides first available for general use by physicians? Martha O'Malley, M.D., Boston.

ANSWER.—The sulfonamides apparently were first available for general use by physicians in Germany in 1936 and in Great Britain, France and the United States in 1937. It is understood that sulfanilamide could be purchased in Boston as early as the middle of November 1936. However, it was a proprietary brand and at that time apparently was not widely distributed.

INTRAVENOUS INJECTIONS

To the Editor:—Is there any more danger in using the saphenous vein at the ankle for intravenous fluids than there is in using the vein of the hand and arm? J. Vernon Pace, M.D., Paducah, Ky.

ANSWER.—In the absence of local contraindication such as varicosities, old thrombophlebitis, phlebothrombosis and the like, and with the body in a horizontal position, fluids may be introduced into any accessible vein without significant difference in risk.

MALARIA

To the Editor:—What proportion of malaria patients are prone to have recurrences and what is the number of permanent cures? In other words, what can be expected as regards the veterans having recurrences and how long will it be necessary for them to continue treatment in order to effect a cure? What is the best accepted treatment of malaria today and the dosage? Leslie C. Taylor, M.D., Lakewood, Ohio.

ANSWER.—An accurate answer to the first question is not possible because the figure is constantly changing. Of the many thousand cases of malaria acquired during the war, relatively few relapses are still occurring. During the war only two types of malaria, falciparum (malignant tertian) and vivax (benign tertian) were of importance. Falciparum malaria is the most severe type and responsible for practically all deaths (which were rare except in prison camps) but has a fortunate biologic characteristic in that after the acute attack it rarely relapses. Vivax malaria, on the other hand, is practically never fatal of itself but will relapse in from 35 to 50 per cent of all instances. With each relapse there is a decreased possibility that another will occur. There is as yet no drug which can be relied on to terminate an infection regardless of amount or duration. The rationale of therapy is to treat each relapse as it occurs and use supportive measures when indicated. Recommended treatment for uncomplicated malaria is atabrine dihydrochloride 0.2 Gm. (3 grains) every six hours for five doses; thereafter 0.1 Gm. (1½ grains) three times daily for five days. It should be taken with fluids, 200 or 300 cc. of water, or before meals in order to reduce gastric irritation.

PERSISTENT HERPES ZOSTER

To the Editor:—A patient has had herpes for three months involving the right lower quadrant of the abdomen. All the known recommended treatments have been tried, including vitamin B, ethyl chloride spray and collodion. I understand that high voltage x-ray therapy has not given satisfactory results. Is there any new treatment for this affliction?

W. J. Klinck, M.D., Lennoxville, Que.

ANSWER.—An additional treatment for herpes is 5 grains (0.32 Gm.) of quinine hydrochloride by mouth three times daily for four days. If no relief is obtained, administration of one ampule of double strength posterior pituitary injection hypodermically daily for two days in succession might be tried. Section of the right tenth, eleventh and twelfth posterior roots of the thoracic spinal cord and right first posterior root of the lumbar spinal cord may be resorted to if other measures fail. Before undertaking such an operation, spinal anesthesia should be administered in order to determine the upper level of the herpetic pain in the thoracic cord.

VALSALVA EXPERIMENT AND PAROXYSMAL TACHYCARDIA

To the Editor:—Will you please explain to me what the Valsalva experiment is, its importance and its use in auricular tachycardia.

William R. Sulman, M.D., Hazleton, Pa.

ANSWER.—The Valsalva experiment consists in an attempted forced expiration with the glottis (or mouth and nose) closed in contrast to the Müller experiment, which is an attempt to inspire forcefully with the glottis closed. The Valsalva experiment increases sharply the intrathoracic pressure and tends to prevent blood from entering the thorax and the heart, with resulting temporary decrease in heart size. There is a vagal reflex effect from this that may act to stop paroxysmal auricular tachycardia. Usually, however, such a therapeutic measure fails, although it is of interest to try it in cases of obstinate auricular paroxysmal tachycardia.

TIME OF DAY FOR METABOLISM TEST

To the Editor:—Basal metabolic tests are done during the morning hours on an empty stomach. Will you kindly advise the reasons, if any, that tests cannot be made during the afternoon?

J. W. Lane, M.D., West Chicago, Ill.

ANSWER.—Basal metabolism determinations are done under so-called basal conditions, namely after a rest period of at least one-half hour and twelve to fourteen hours after the last meal. The digestion of food raises the basal metabolism somewhat, particularly protein food, because of its specific dynamic action.

There is no good reason why under some circumstances basal metabolism tests should not be done in the afternoon if the program of the patient is arranged in such a way that he sleeps later in the morning. For most patients the afternoon would be an unsatisfactory time because work and the emotional stress and strain of ordinary daily events might raise the metabolism even though it was preceded by the usual rest period.

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